velopex INTERNATIONAL

sylc.™

POWERED BY NOVAMIN.

Contents

sylc® Therapeutic Prophy Powder

POWERED BY **NOVAMIN®**

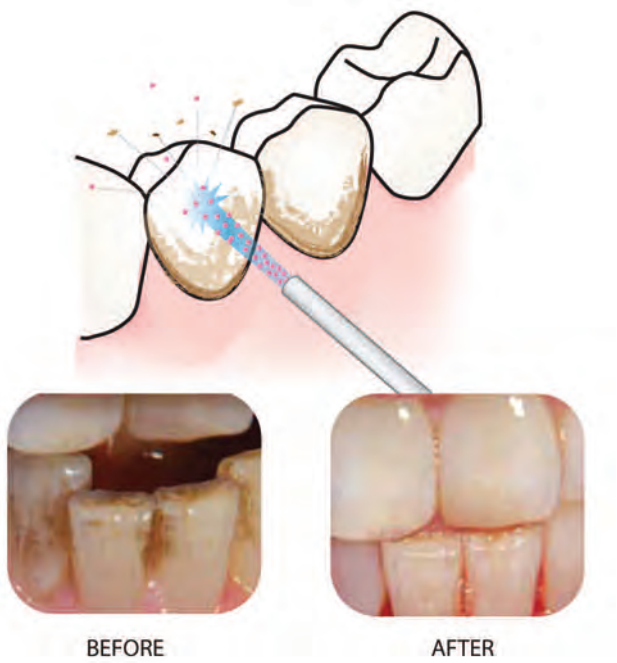
What does it do?

High level, Fast cleaning[1,2,3]

Fast Desensitizing[4]

Increased Patient Comfort[5]

Protect and Soothe[6,7]



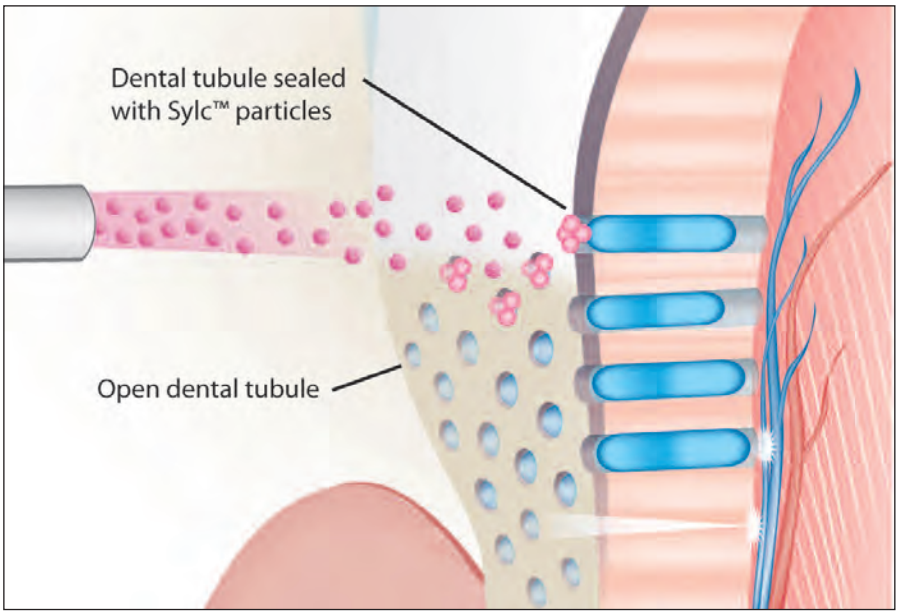
How does it work?

Sylc's protective and soothing ability comes from Novamin.

NovaMin is calcium sodium phosphosilicate, which seeks out and forms a tooth-like layer over vulnerable areas of the tooth where dentine is exposed.

When combined with saliva or water, Sylc forms hydroxycarbonate apatite crystals (HCA) that increase the natural protective and repair mechanisms of saliva.

Unlike traditional desensitising varnishes or pastes, Sylc provides superior relief from painful hypersensitivity without unsightly discolouration or unpleasant taste or feel.



Illustrations are interpretive depictions for informational purposes only.

available at www.sciencedirect.com
ScienceDirect
journal homepage: www.intl.elsevierhealth.com/journals/jden

A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air-polishing powders

A. Banerjee *, *M. Hajatdoost-Sani*, *S. Farrell*, *I. Thompson*

King's College London Dental Institute, KCL, United Kingdom

ARTICLE INFO

Article history:
Received 20 July 2009
Received in revised form
16 February 2010
Accepted 2 March 2010

Keywords:
Bioactive glass
Sodium bicarbonate
Air-abrasion
Air-polishing
Dental sensitivity
Staining
Discolouration
Shade

SUMMARY

Objective: Compare clinical effectiveness of sodium bicarbonate and bioactive glass powders used for dental prophylaxis.

Methods: 25 patients were allocated to either good or poor oral hygiene subgroups ($n = 50$). Using a double-blind, split-mouth model, all patients underwent prophylaxis treatment on mandibular teeth; maxillary teeth were untreated controls. Bioactive glass (Sylc, OSspray Ltd., UK) and sodium bicarbonate (Prophy Jet, Dentsply, UK) were applied randomly to opposite sides of each mouth. Sensitivity to cold air/ethyl chloride, dental shade change and procedural comfort were measured. All parameters were recorded immediately pre- and post-treatment and at 10-day recall.

Results: Bioactive glass air-polishing, in both subgroups, reported a 44% (0.80 ± 0.10, $p < 0.05$) decrease in dental sensitivity, against controls, immediately after application, and a 42% (0.85 ± 0.05, $p < 0.05$) decrease at 10-day recall when stimulated with cold air. Ethyl chloride stimulation showed a 10% (3.05 ± 0.17, $p < 0.05$) and 22% (2.64 ± 0.33, $p < 0.05$) reduction in sensitivity immediately post-op and at 10-day recall. Application of sodium bicarbonate powders increased sensitivity, 17% (1.76 ± 0.3, $p < 0.05$), at 10 days when stimulated with cold air. Both powders showed variation between subgroups in colour change, bioactive glass powder 1 and 4 shades whiter, sodium bicarbonate 1 and 2 shades whiter in good and poor oral hygiene groups, respectively. Patients in both subgroups reported a 46% (7.9 ± 1.4, $p < 0.05$) increase in comfort of procedure with the bioactive glass over that when using sodium bicarbonate.

Conclusions: Bioactive glass air-polishing was more clinically and statistically effective at desensitising both good and poor oral hygiene groups, and removing stain in the poor oral hygiene patient subgroup. Bioactive glass also provided better overall patient comfort during the procedure.

1. Introduction

The air-polishing of teeth has traditionally been achieved with sodium bicarbonate powders in order to remove extrinsic staining on teeth. This operator-sensitive procedure can lead to excessive abrasion on the exposed dentine surfaces, often resulting in patients experiencing increased dental sensitivity post-operatively. Consequently, dental practitioners and hygienists are reluctant to use air-polishing powders on patients who have existing dental hypersensitivity.[1] Dental hypersensitivity is a clinical problem that affects approximately 40 million adults in the United States, 10 million of

* *Corresponding author at*: Floor 26, Tower Wing, Guy's Dental Hospital, London Bridge, London, SE1 9RT, United Kingdom. Tel.: +44 0207 188 1577; fax: +44 0207 188 7486.
E-mail address: avijit.banerjee@kcl.ac.uk (A. Banerjee).
0300-5712/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jdent.2010.03.001

which can be considered chronically affected. It is estimated that some 17% of adults in the U.S. have at least one or more sensitive teeth.[2] It has been reported in a UK study that the prevalence of dentine sensitivity in a large cohort of general practice patient was lower at 4%.[3] The variation in prevalence rates may reflect differing study designs.

The generally accepted basis for the physiological cause of dentine hypersensitivity is Brännström's hydrodynamic theory.[4] This concept states that exposed, open dentinal tubules at the tooth surface permit dentinal fluid movement along the tubules which in turn, excites the nerve endings in the subodontoblastic nerve plexus in the dental pulp, so causing acute discomfort.

There are many approaches to the treatment and prevention of dentinal hypersensitivity. Treatment of the tooth with a chemical agent that penetrates into the dentinal tubules and depolarizes the nerve synapse, so reducing sensitivity by preventing the conduction of pain impulses, is a method used in daily use toothpastes (e.g., potassium nitrate).[5,6] An alternative approach is to treat the tooth with a chemical or physical agent that creates a layer that mechanically occludes the exposed dentinal tubules, thus reducing sensitivity by preventing dentinal fluid flow—a method used by prophylaxis pastes and varnishes (e.g., potassium oxalate, ferric oxalate).[7,8] Although both approaches are effective at reducing or eliminating hypersensitivity, the duration of the relief is variable. Dentine hypersensitivity usually reoccurs due to abrasion from excessive tooth brushing, chemical erosion, or mechanical failure of the coating material.[9] Therefore, there is a need for dental materials that can chemically react with dental tissues, adhering to tooth structure, so significantly reducing the possibility of reopening occluded tubules. Progress has been made towards meeting this need through the development of materials that deposit calcium phosphate onto the tooth surface to mechanically occlude exposed dentinal tubules. Commercially available products such as Tooth Mousse (GC, USA) and NovaMin (NovaMin Technologies, USA) provide such ions for remineralisation.[10–12] A novel cleaning and desensitising prophy-powder, based on bioactive glass technology, has been developed (OSspray Ltd., UK) which aims to occlude open dentine tubules, whilst leaving calcium phosphate ions adhered to the surface in a single application via an air-polishing treatment.

The null hypothesis investigated in this in vivo study was that bioactive glass air-polishing has the same clinical effectiveness of desensitisation of exposed dentine, extrinsic stain removal and procedural comfort when compared to using conventional sodium bicarbonate air-polishing techniques.

2. Materials and methods

Fifty patients were recruited from Kings College London Dental Institute with appropriate ethics approval (Bromley REC: 07/H0805/24). Twenty-five patients were allocated to either a low or high oral hygiene subgroup determined by pre-operative plaque scores and clinical examination. Inclusion/exclusion criteria were as follows:

Inclusion criteria:

1. Male or female patient; 18–64 years old.
2. Patient has relevant teeth present for the study (incisors and first premolars) and these are unrestored and the patient is not wearing dentures.
3. Patient is able to give informed consent.
4. Patient's maxillary teeth to be included in the study will have a shade of C1 or darker, as determined by clinician, using the standard Vita value-ordered shade guide.

Exclusion criteria:

1. Orthodontic appliance treatment within the last three months.
2. Periodontal surgery within the last 3 months.
3. Crowns or abutments on upper right or left central incisors, upper right or left central laterals, or upper right or left canines.
4. Patients receiving radiation or chemotherapy.
5. Patients having undergone dental prophylaxis within the last 3 months.
6. Previous history of dental bleaching procedures.
7. Known allergy to silica.

Using a double-blinded, split-mouth model, all patients underwent a full prophylaxis treatment on the mandibular teeth. Air-polishing therapies were applied until a clinically significant clean was complete or until additional treatment would no longer result in any additional improvement in cleaning judged clinically. All treatments were applied for a minimum of 20 s. All powders were applied using a Dentsply Cavitron Jet air-polishing device (Dentsply, USA). Bioactive glass (Sylc, OSspray Ltd., UK) and sodium bicarbonate (Prophy Jet, Dentsply, UK) were applied randomly to opposite sides of the mandibular dentition. The maxillary dentition was left as the untreated control in each patient. Three parameters were measured:

(1) *Sensitivity to cold air and ethyl chloride*: Prior to any treatment the patient's response to cold air was measured. Cold air via a 3-in-1 hand piece was applied to the tooth surface at a distance of approximately 1 cm for three seconds. Lower left 1, 2, 4, lower right 1, 2, 4 and upper right 1, 2, and 4 were measured using a VAS Scale (Fig. 1). After a delay of 5 min, the same procedure was used but ethyl chloride (''Glacier'' Produits Dentaires, Vevey, Switzerland) was applied via a cotton wool swab to the dried buccal surface of each tooth for 3 s. The order of tooth application was randomised. The two tested, blinded prophylaxis treatments were then applied to randomly assigned sides of the lower dentition in each patient. Sensitivity to cold air and ethyl chloride was then re-measured immediately post-treatment using the same pre-treatment protocols.
(2) *Shade change*: Prior to any treatment, tooth shade was measured using an intra-oral spectrophotometer, Vita Easyshade (Vivadent, USA). The spectrophotometer was calibrated as per manufacturer's instructions and was used to measure the shade of the following teeth: lower left 1, 2, 4, lower right 1, 2, 4 and upper right 1, 2, and 4 (both test

Please cite this article in press as: Banerjee A, et al. A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air-polishing powders. J Dent (2010), doi:10.1016/j.jdent.2010.03.001

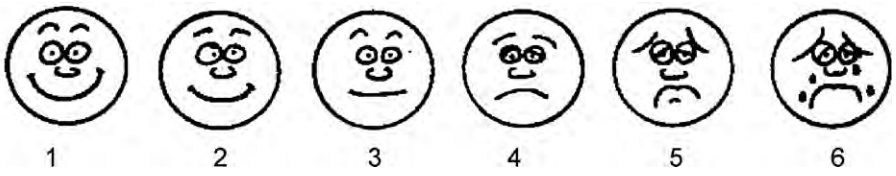


Fig. 1 – Visual analogue scale to measure dental pain. Patients must choose one from the scale of six images to express their level of discomfort.

teeth and controls in each patient). The two tested, double-blinded prophylaxis treatments were then applied to randomly assigned sides of the lower dentition in each patient. Dental surface shade was then re-measured immediately post-treatment using the same pre-treatment protocol.

(3) *Comfort of procedure*: Immediately post-treatment, patients were asked to rate their overall experience of each double-blinded prophy treatment. A 10-point linear scale was used, 1 = bad experience through to 10 = good experience. All 50 patients were recalled to the surgery 10 days post-operatively for a follow up consultation. Sensitivity to cold air and ethyl chloride as well as the tooth shade were re-measured using the methods previously described.

Data was statistically analysed using Students paired *t*-test.

3. Results

3.1. *Sensitivity to cold air and ethyl chloride*

Analysis of bioactive glass data reported a 44% (±10%) reduction in sensitivity to cold air stimulus immediately post-treatment. The reduction in cold air sensitivity was maintained at the 10-day follow up at 42% (±5%). Both results were statistically significant from the pre-treatment controls ($p < 0.05$). The sodium bicarbonate data showed a small reduction is sensitivity but this was not significant to the pre-treatment controls. The 10-day follow up reported a statistically significant ($p < 0.05$) 17 ± 15% increase in sensitivity to cold air (Fig. 2).

Application of ethyl chloride to the bioactive glass treated surface showed a statistically significant drop in sensitivity, 10% (±5%) ($p < 0.05$). However, at 10-day follow up the sensitivity had dropped to 22% (±12%) ($p < 0.05$). Sodium bicarbonate treated surfaces showed no significant difference in sensitivity when stimulated with ethyl chloride (Fig. 3).

Students paired *t*-test analysis of the cold air and ethyl chloride stimulus data showed no statistical difference in sensitivity between the two test and one control areas in each of the patients' mouths, pre-treatment. Nor was there any statistical change in sensitivity in the control area of the mouth over the duration of the trial.

Analysis also showed no statistical difference in sensitivity for both good and poor oral hygiene groups throughout the trial.

3.2. *Shade change*

Both test powders showed variation between good and poor oral hygiene subgroups. Tables 1 and 2 show the mean starting shade (good OH group: shade B1 and poor OH group: shade C2), and the relative lighter shade immediately post-treatment and at 10-day follow up. It appeared from the data sets, that the effect of Bioglass air-polishing was to lighten the shade by at least one further tab than the equivalent sodium bicarbonate treatment in the patients with poor oral hygiene.

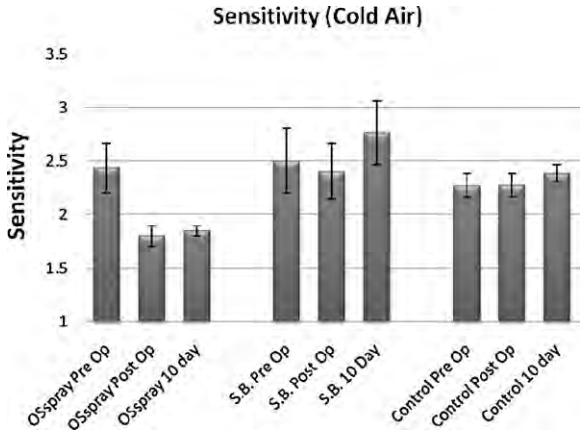


Fig. 2 – Data showing changes in sensitivity to cold air pre- and post-treatment and at the 10-day follow up (measured using VAS). Statistically significant reductions in dentine sensitivity were found in the Bioglass group alone (OSspray) with an increase shown in the 10-day follow up with sodium bicarbonate (SB).

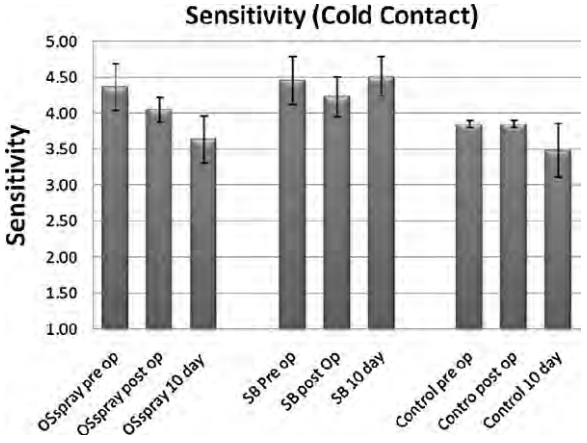


Fig. 3 – Data showing the statistically significant drop in sensitivity (measured using VAS) elicited by ethyl chloride contact in the Bioglass treatment group (OSspray) post-op and after the 10-day follow up. No other statistically significant differences were found.

Please cite this article in press as: Banerjee A, et al. A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air-polishing powders. J Dent (2010), doi:10.1016/j.jdent.2010.03.001

Table 1 – Good oral hygiene subgroup. Patients started out with shade B1 and after 10-days both groups elicited a lightening effect, measured using the spectrophotometer.

	Pre-op	Immed post-op	10 Days post-op
Bioactive glass ($n = 25$)	B1	−2	−1
Sodium bicarbonate ($n = 25$)	B1	−1	−1

Table 2 – Poor oral hygiene subgroup. In this group of patients, it appeared that the Bioglass treatment lightened the dental shade further after 10 days.

	Pre-op	Immed post-op	10 Days post-op
Bioactive glass ($n = 25$)	C2	−4	−3
Sodium bicarbonate ($n = 25$)	C2	−2	−2

Table 3 – Data showing patient comfort differences between Bioglass and sodium bicarbonate treatments. There is a statistically significant difference in patient experience between the two procedures ($p < 0.01$, Students paired t-test).

	Mean	SD	
Bioactive glass	7.9	1.4	$n = 50$
Sodium bicarbonate	5.4	2.0	$n = 50$

3.3. *Comfort of procedure*

Patients treated with bioactive glass, in both subgroups reported a $46 \pm 18\%$ ($p < 0.05$) increase in comfort of procedure with the bioactive glass over that of sodium bicarbonate (Table 3).

4. Discussion

The marked differences in the dentine sensitivity data indicates the two tested air-polishing powders behave in differently in their interaction with the exposed dentine surface. Initially the sodium bicarbonate occluded some tubules, so reducing immediate post-operative sensitivity, but after 10 days the soluble sodium bicarbonate dissolved in the oral cavity and so the sensitivity increased. However, the bioactive glass composed of elements that occur naturally in the body's hard tissues (calcium sodium phosphosilicate), when exposed to an aqueous environment undergoes a surface reaction over several hours, allowing it to physically adhere to exposed dentine and to physically occlude tubules. Within a short period of time, essentially all of the bioactive glass particles react to form hydroxycarbonate apatite (HCA), which is chemically and structurally similar to natural tooth mineral.[10–12] This leads to a more long-term reduction in dentine hypersensitivity as this material is less easily degraded and removed in the oral cavity. It is also possible that the relative alkalinity of the bioactive glass-dentine interface may help neutralise, to a degree, the surface effect of dietary acids which may contribute to clinical dental hypersensitivity in some patients.

The relative increase in sensitivity associated from cold air and ethyl chloride stimulation was expected. However, the level of desensitisation from the bioactive glass would suggest these particles seal the exposed tubules sufficiently well so that the cold and physical movement of the air cannot penetrate the tubule structure. The increased stimulation from the much colder iced cotton wool swab is still reduced with bioactive glass at post-treatment testing (10%) but the closure of the tubule structure is not complete until the bioactive glass has been able to convert to the HCA structure hence a greater (20%) reduction in sensitivity.

The shade changes differing between poor and good oral hygiene groups were expected. The lower the level of oral hygiene can be associated with greater levels of extrinsic staining. Both air-polishing powders were more effective at improving whiteness on already stained teeth. The bioactive glass powders appeared to be a better stain removal system than the sodium bicarbonate, due to the fact that these particles have greater density and a more spherical aspect ratio than the sodium bicarbonate, so making them more efficient physical stain-removers.

Patient comfort data showed a very clear improvement in the acceptance of the procedure when using bioactive glass powders. The comments regarding sodium bicarbonate's taste and 'stinging of soft tissue' effects are key drivers in the low patient acceptance of air-polishing with conventional sodium bicarbonate as a prophylaxis technology.

Limitations of the present investigation included the relatively low number of patients included within the study suffering from relatively low levels of dentine sensitivity pre-operatively. However, even with this patient number, both clinical and statistical differences were highlighted indicating that adequate numbers had been used to indicate differences between the two systems. The 10-day follow up period was used both as a clinical indicator and for study convenience, but it might be prudent in future to assess the effects further long-term in patients with higher levels of pre-operative dentine sensitivity. It was appreciated that although the clinicians were blinded as to which powder was used, once the procedure was under way, it would be evident which powder dissolved. The powders were blindly randomised to try to reduce operator bias.

5. Conclusions

Within the limits of this study, the null hypothesis was disproved. The bioactive glass powder had a significant longer term desensitising effect, whereas the sodium bicarbonate powders tended towards increasing dentine sensitivity. The bioactive glass appeared to offer a more effective whitening effect when compared to sodium bicarbonate. The bioactive glass system also provided a more acceptable patient experience. Thus the bioactive glass powder may afford a more acceptable clinical experience for professional dental stain removal with a significant added benefit of reducing dental sensitivity.

Please cite this article in press as: Banerjee A, et al. A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air-polishing powders. J Dent (2010), doi:10.1016/j.jdent.2010.03.001

Acknowledgements

Materials for this study were kindly provided by OSspray Ltd. The authors would like to thank Shameem Sharriff for her role as dental nurse/trial co-ordinator.

REFERENCES

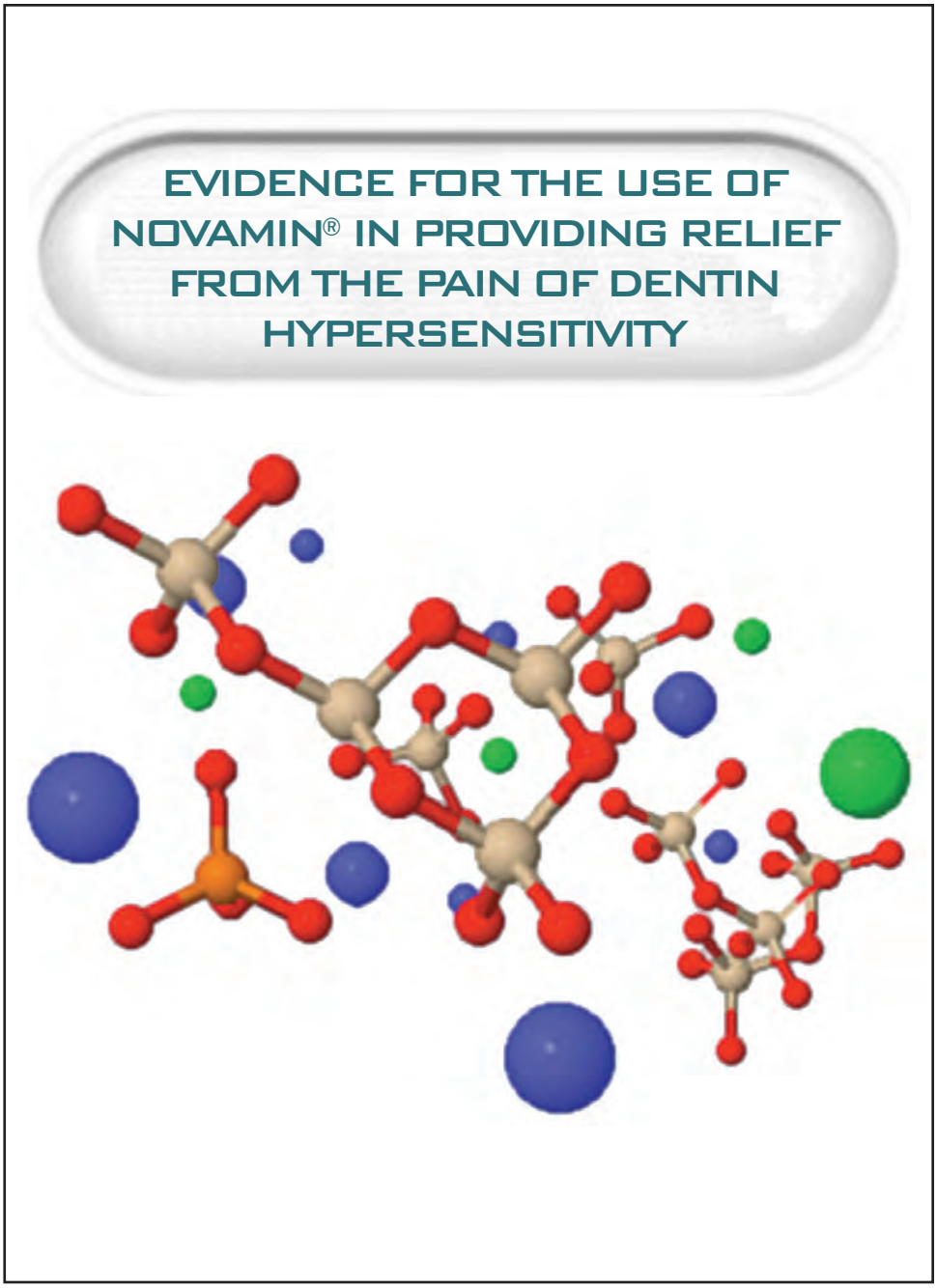
1. Gutmann ME. Airpolishing: a comprehensive review of the literature. *Journal of Dental Hygiene* 1998;**72**:47–56.
2. Coleman TA, Kinderknecht KE. Cervical dentin hypersensitivity. Part I: The air indexing method. *Quintessence International* 2000;**31**:461–5.
3. Rees JS, Addy M. A cross-sectional study of dentine hypersensitivity. *Journal of Clinical Periodontology* 2002;**29**:997–1003.
4. Brännström M, Astrom A. The hydrodynamics of the dentine; its possible relationship to dentinal pain. *International Dental Journal* 1972;**22**:219–27.
5. Markowitz K, Kim S. The role of selected cations in the desensitization of intradental nerves. *Proceedings of the Finnish Dental Society* 1992;**88**:39–54.
6. Schiff T, Dos Santos M, Laffi S, Yoshioka M, Baines E, Brasil KD, *et al*. Efficacy of a dentifrice containing 5% potassium nitrate and 1500 PPM sodium monofluorophosphate in a precipitated calcium carbonate base on dentinal hypersensitivity. *Journal of Clinical Dentistry* 1998;**9**:22–5.
7. Orchardson R, Gillam DG. The efficacy of potassium salts as agents for treating dentin hypersensitivity. *Journal of Orofacial Pain* 2000;**14**:9–19.
8. Dragolich WE, Pashley DH, Brennan WA, O'Neal RB, Horner JA, Van Dyke TE. An in vitro study of dentinal tubule occlusion by ferric oxalate. *Journal of Periodontology* 1993;**64**:1045–51.
9. Kozlovsky A, Soldinger M, Sperling I. The effectiveness of the air-powder abrasive device on the tooth and periodontium: an overview. *Clinical Prevention in Dentistry* 1989;**11**:7–11.
10. Reynolds EC. The prevention of sub-surface demineralization of bovine enamel and change in plaque composition by casein in an intra-oral model. *Journal of Dental Research* 1987;**66**:1120–7.
11. Featherstone JDB, Zero DT. An in situ model for simultaneous assessment of inhibition of demineralization and enhancement of remineralization. *Journal of Dental Research* 1992;**71**:804–10.
12. Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J, *et al*. Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (NovaMin) for the treatment of dentin hypersensitivity. *American Journal of Dentistry* 2008;**21**:210–4.

Please cite this article in press as: Banerjee A, et al. A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air-polishing powders. J Dent (2010), doi:10.1016/j.jdent.2010.03.001

The
Journal of Clinical Dentistry®
THE INTERNATIONAL JOURNAL OF APPLIED DENTAL RESEARCH
www.JClinDent.com

Volume XXI **2010** **Number 3**

Special Issue



The Journal of Clinical Dentistry (ISSN 0895-8831) is published by Professional Audience Communications, Inc., P.O. Box 243, Yardley, PA 19067. POSTMASTER; Send address changes to P O. Box 243, Yardley, PA 19067.

On the Cover

The molecular structure of a fragment of NovaMin, showing the atoms of calcium (green), sodium (blue), phosphorous (orange), silica (beige), and oxygen (red).

The Journal of Clinical Dentistry has been accepted for inclusion on MEDLINE, the BIOSIS, SCISEARCH, BIOMED and EMBASE databases, and the Automatic Subject Citation Alert.

Contents

NovaMin® Technology

Randy Scott

NovaMin Technology Inc.
Alachua, FL, USA

(J Clin Dent 2010;21[Spec Iss]:59–60)

In 2003, NovaMin Technology Inc. was formed to commercialize a novel compound, termed calcium sodium phosphosilicate, for use in oral healthcare. This Special Issue of *The Journal of Clinical Dentistry* charts the history of calcium sodium phosphosilicate from a material originally developed for bone regeneration, to an effective ingredient for the treatment of dentinal hypersensitivity.

Calcium sodium phosphosilicate was invented by Professor Larry Hench at the University of Florida in the late 1960s, and originally found utility in the development of new bone-regeneration materials.[1] Later, in the mid-1990s, Drs. Leonard Litkowski, Gary Hack (both at the University of Maryland at that time) and David Greenspan adapted the material for dentin remineralization.

Calcium sodium phosphosilicate, or NovaMin® as it is referred to under its trade name, is an inorganic, amorphous melt-derived glass compound that contains only calcium, sodium, phosphate, and silica. NovaMin has been employed as an ingredient in oral healthcare products around the globe for the alleviation of dentinal hypersensitivity for nearly 10 years; it can now be found in a range of oral healthcare preparations, such as prophylaxis paste and toothpaste. Since 2003, NovaMin Technology Inc. conducted a number of studies of significant scientific value to confirm both the mechanism of action of NovaMin, and its efficacy in providing relief from the pain of dentin hypersensitivity.

In 2010, NovaMin Technology Inc. was acquired by GlaxoSmithKline. This Special Issue has been funded by GlaxoSmithKline to make publicly available, in a single consolidated peer-reviewed publication, much of the NovaMin Technology Inc.-sponsored and supported research on calcium sodium phosphosilicate and its effects on dentinal hypersensitivity.

In the first article of this Special Issue, Dr. Greenspan discusses the history of calcium phosphosilicate as a potential bone implant material, and its evolution to NovaMin as an effective treatment for the relief of pain associated with dentin hypersensitivity.[2] The article highlights unique parallels between the repair of damaged bones and the repair of dental hard tissue.

The next two articles explore the mechanistic role of NovaMin in repairing exposed dentin. Burwell, *et al.*[3] successfully demonstrated that NovaMin is attracted to an exposed dentin surface and forms a mineralized layer. This study is in agreement with the earlier work by Hench,[1] but is a first on dentin. In a further *in vitro* study, LaTorre and Greenspan[4] were able to characterize the release rate of ions from NovaMin under physiological conditions, and were able to demonstrate, again for the first time, integration of the calcium and phosphate ions released from NovaMin into a reparative layer over dentin.

Supported by very strong mechanistic understandings, NovaMin has also demonstrated clinical efficacy. Litkowski and Greenspan,[5] in a randomized, double-blind, placebo-controlled proof of principle clinical study, demonstrated the effectiveness of two prototype dentifrice formulations containing NovaMin compared to a placebo dentifrice. This was the first study to support the efficacy of a dentifrice incorporating NovaMin for the treatment of dentin hypersensitivity. With further refinement, the prototype formulations evolved into fully developed dentifrice formulations containing 5% w/w NovaMin.

Salian, *et al.*[6] explored the clinical efficacy of a 5% NovaMin dentifrice compared to a 5% potassium nitrate-containing toothpaste and a non-desensitizing dentifrice in a four-week double-blind clinical study. The results demonstrated that the use of a dentifrice containing NovaMin provided rapid, and significantly more relief from the pain of dentin hypersensitivity compared to a dentifrice containing 5% potassium nitrate and a negative control at four weeks.

The final paper in this Special Issue presents a randomized, double-blind clinical study comparing a NovaMin dentifrice to a potassium nitrate dentifrice and a stannous fluoride dentifrice. The study, by Sharma, *et al.,*[7] demonstrated unequivocally that NovaMin is effective and could provide substantial and significant improvements in sensitivity relief at early time points. In recent years, a number of clinical trials, not supported by NovaMin Technology Inc., have been published.[8-10] These double-blind randomized clinical trials have also demonstrated superior reductions in dentin hypersensitivity for NovaMin-containing dentifrices compared to a placebo control dentifrice,[8] or a placebo dentifrice and potassium nitrate dentifrice.[9]

The research described in this Special Issue provides scientific support and understanding as to the mechanisms and efficacy of NovaMin-containing oral healthcare products.

Thank you to those people who have been instrumental in the development and commercialization of this groundbreaking technology. First, the NovaMin Technology Inc. team who pioneered the development of the ingredient for oral healthcare use, and conducted research to confirm its mode of action and effectiveness as a treatment for dentinal hypersensitivity. I would particularly like to thank the core team members Guy La Torre, David Greenspan, and Anora Burwell, all whom have authored papers in this Special Issue.

Finally, to GSK, my thanks to Dr. Teresa Layer, Vice President Sensodyne Research and Development, for providing the opportunity and resources to enable this important Special Issue to be published.

References

1. Hench LL. Biomaterials. *Science* 1980; 208:826-831.
2. Greenspan DC. Novamin and tooth sensitivity: An overview. *J Clin Dent* 2010;21(Spec Iss):61-65.
3. Burwell A, Jennings D, Muscle D, Greenspan DC. NovaMin and dentin hypersensitivity—*In vitro* evidence of efficacy. *J Clin Dent* 2010;21(Spec Iss):66-71.
4. LaTorre G, Greenspan DC. The role of ionic release from NovaMin (calcium sodium phosphosilicate) in tubule occlusion: An exploratory *in vitro* study using radio-labeled isotopes. *J Clin Dent* 2010;21(Spec Iss):72-76.
5. Litkowski L, Greenspan DC. A clinical study of the effect of calcium sodium phosphosilicate on dentin hypersensitivity—Proof of principle. *J Clin Dent* 2010;21(Spec Iss):77-81.
6. Salian S, Thakur S, Kulkarni S, LaTorre G. A randomized controlled clinical study evaluating the efficacy of two desensitizing dentifrices. *J Clin Dent* 2010;21(Spec Iss):82-87.
7. Sharma N, Roy S, Kakar A, Greenspan DC, Scott R. A clinical study comparing oral formulations containing 7.5% calcium sodium phosphosilicate (NovaMin), 5% potassium nitrate, and 0.4% stannous fluoride for the management of dentin hypersensitivity. *J Clin Dent* 2010;21(Spec Iss): 88-92.
8. Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J, Tai BJ. Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (NovaMin) for the treatment of dentin hypersensitivity. *Am J Dent* 2008;21:210-214.
9. Pradeep AR, Anuj SJ. Comparison of the clinical efficacy of a dentifrice containing calcium sodium phosphosilicate with a dentifrice containing potassium nitrate and a placebo on dentinal hypersensitivity: A randomized clinical trial. *J Periodontol* 2010;81:1167-1173.
10. Narongdej T, Sakoolnamarka R, Boonroung T. The effectiveness of a calcium sodium phophosilicate desensitizer in reducing cervical dentin hypersensitivity: A pilot study. *J Am Dent Assoc* 2010;141:995-999.

NovaMin® and Tooth Sensitivity—An Overview

David C. Greenspan, PhD

Spinode Consulting
Gainesville, FL, USA

(J Clin Dent 2010;21[Spec Iss]:61–65)

Introduction

NovaMin® is the branded ingredient found in a number of professional use and over-the-counter dental products designed to give immediate and long-lasting relief from tooth sensitivity. NovaMin is technically described as an inorganic amorphous calcium sodium phosphosilicate (CSPS) material that was designed based on a class of materials known as bioactive glasses. The particular composition of NovaMin (also referred to as 45S5) is identical to that of the best known bioactive glass material, Bioglass®, and contains only calcium, sodium, phosphate, and silica, all as an amorphous matrix. NovaMin and the other CSPS materials were originally developed as bone regenerative materials in the early 1970s. CSPS materials were part of a broader class of bioactive ceramics, which included calcium phosphate materials and calcium hydroxyapatite materials, developed for hard tissue repair and replacement, mainly due to their chemical similarity to bone mineral.[1] It is instructive to understand the science behind the unique properties and reactivity of the CSPS materials, and how the science that was developed for bone regenerative medicine translated directly to the area of oral healthcare. Specifically, this article briefly reviews the history of the development of this novel class of biomaterial, and describes the mode of action of CSPS that results in its performance in the reduction of tooth sensitivity by physically occluding dentin tubules.

Early Development of CSPS (Bioactive Glass) Materials

Until the time of the invention of this class of materials, all biomaterials were made to be as inert as possible in the human body.[2] The initial animal studies with the original CSPS composition (the same composition as NovaMin) demonstrated for the first time that a synthetic biomaterial could actually form a direct chemical bond with bone tissue.[3] These early implants were able to bridge a gap when a section of bone was missing. The ends of the bone were found to firmly bond to the bioactive glass surface.[4] At the time of this discovery, there were significant needs to find better therapies to repair severe limb trauma and to fix metallic orthopedic implants. The seminal discovery that a synthetic biomaterial could form a chemical bond with bone allowed researchers to change their view of how biomaterials could be engineered to interact with the body, rather than finding ways to minimize the interactions between the body and the implanted materials.

Research during the years following this discovery focused on analyzing the bond between the bone tissue and the CSPS material, and how this bond formed. Various investigators found that the CSPS material actually went through a series of reactions at the surface of the material that released ions into the surroundings, and that the surface of the CSPS material changed in composition and structure.[5] These are summarized in Table I. Specifically, these materials have been found to react when placed into an aqueous environment, releasing specific ions into the solution. Studies have shown that sodium is rapidly released from the surface of the material, creating a surface that is depleted in this ion.[6] This reaction, which begins immediately upon exposure of the material to the aqueous environment, then allows calcium from the material to diffuse into the surroundings. The net effect of these reactions is a surface that is essentially rich in silica, and has a very porous surface. Furthermore, in a closed system, such as is found in most *in vitro* studies, the pH of the solution was found to increase from a neutral pH to a basic pH. The extent of the pH rise was found to be related to the buffer strength of the solution, the surface area to volume ratio of the particles, and the composition of the starting CSPS.

Table I
Reaction Sequence for CSPS Materials

1. Rapid exchange of Na^+ in the glass with H^+ in solution; pH rise;
2. Loss of soluble silica as $Si(OH)_4$ by breaking of Si-O-Si bridges and the subsequent formation of surface silanol groups in the process; creates 3-member SiO_2 chains;
3. Condensation and repolymerization of surface silanols to form an SiO_2-rich surface layer;
4. Migration of Ca^{++} and PO_4^{3-} to the surface through the silica-rich layer and the formation of a Ca-P-rich layer on the surface of the glass;
5. Incorporation of OH^-, CO_3^{2-} from the solution and the subsequent crystallization of the Ca-P layer to form HCA.

These initial reactions result in the surface of the CSPS particle becoming negatively charged. This surface charge facilitates the adsorption of proteins, as well as calcium and phosphate ions from the solution. Over a period of hours, a carbonated calcium hydroxyapatite mineral (HCA) phase will form on the surface of the material, and this becomes the bonding interface. The net effect of these reactions confirms the mechanism of the bonding interface between the implant surface and bone. This was dramatically shown in early histology images, such as those in Figure 1. Here it is evident that bone cells have attached to a calcium phosphate-rich layer (C) and underneath that layer is the silica rich layer.[4]

More recently, a series of investigations has demonstrated that this specific composition of CSPS material can stimulate and accelerate bone repair and early angiogenesis compared with other bioactive ceramic compounds.[7,8] In addition, it was found that simply exposing bone tissue to the ionic reaction products from the 45S5 composition resulted in accelerated bone cell proliferation and maturation, as well as enhanced rates of new blood vessel formation.[9] The mechanisms associated with these

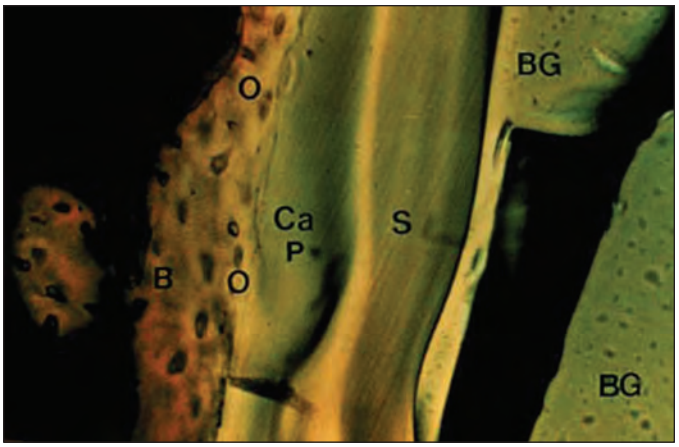


Figure 1. *This figure shows the bonding interface of CSPS, 45S5 bioactive glass taken from a 3-month implant in a rat tibia. BG = bioactive glass, S = silica rich layer, CaP = calcium phosphate layer, O = osteoblasts, B = new bone formation. (Courtesy of Prof. Larry Hench)*

properties appear to be directly related to the amount and rate of ionic release from these materials.[10] These studies have resulted in a better understanding of the importance of the kinetics and relative critical amounts of ions released from this CSPS composition, and the relation of these reactions to accelerated bone healing.

Due to increasing commercial use of these materials in the 1990s, especially particulate CSPS materials for treating periodontal bone defects and for orthopedic bone defects, research intensified in the area of characterization of the reactions of small particles of CSPS materials. While it is beyond the scope of this paper to go into great detail about these works, it had become clear that the size distribution of particles and the concentration of particles have a significant effect on the reactivity of the material.[11-13] Because smaller particles have a greater surface area for a given volume of material, it was found that size and concentration of particles were critical in obtaining optimal results in surgical situations. In addition, these studies demonstrated that the effects of particle size would cause different changes in the pH of the reaction solutions, and that the reactions would proceed to varying degrees of completion, depending on the ratio of the surface area of particles to volume of solution.

Interestingly, the reactivity of small particles of the CSPS materials has been shown to result in some antimicrobial properties against oral bacteria,[14,15] as well as have some transient anti-inflammatory properties.[16] These properties were somewhat unexpected; however, the positive attributes found *in vitro* help to explain the very positive clinical results with these materials. In addition to these studies, new analytical techniques allowed for more detailed *in vitro* experiments that have shown how the ionic reactions and resultant surface modifications beneficially interact with collagen, allowing for strong bonding between collagen and the surfaces of these materials.[17,18] It was the combination of all of these factors that led to the development of NovaMin for the treatment of tooth sensitivity.

NovaMin and Sensitivity Mode of Action

The currently accepted theory for tooth hypersensitivity is the hydrodynamic theory developed by Brännström and Aström.[19] The premise of the hydrodynamic theory is the belief that open dentinal tubules allow fluid flow through the tubules, which excites the nerve endings in the dental pulp. Clinical replicas of sensitive teeth viewed under a scanning electron microscope (SEM) reveal varying numbers of open or partially occluded dentinal tubules.[20] These studies have also shown that in patients with dentin hypersensitivity, there are a greater number of tubules per area and the diameter of the tubules is greater than in patients with no sensitivity.[21] In general, tubules are not exposed at the tooth root surface because of the cementum covering the tooth root, or because of a smear layer of dentinal debris that covers the tooth surface and masks the tubules. When the smear layer is present, the fluid flow that can occur through the dentin is only a few percent of that possible following acid removal of the smear layer, which opens the tubules.

There are two basic approaches to the treatment of dentinal hypersensitivity. The first approach is to treat the tooth with a chemical agent, such as potassium nitrate or potassium chloride, that penetrates into the dentinal tubules and depolarizes the nerve synapse, which reduces sensitivity by preventing the conduction of pain impulses.[22] There have been numerous clinical studies that have tested the efficacy of these agents to reduce dentin hypersensitivity. While these materials have consistently shown clinical efficacy in the treatment of sensitivity, it may take weeks for the patient to perceive a reduction in pain and sensitivity. The second approach is to treat the tooth with a chemical or physical agent, such as potassium oxalate, ferric oxalate, or strontium chloride, to physically occlude dentinal tubules, which reduces sensitivity by prevention of tubule fluid flow.[23] Although both approaches are effective at reducing or eliminating hypersensitivity, the duration of relief is highly variable. Hypersensitivity usually reappears due to toothbrush abrasion, the presence of acid challenges in the mouth, and/or degradation of the coating material.[24]

The use of CSPS in periodontal surgery,[25] where tooth sensitivity is routinely found, coupled with the need for improved materials to treat tooth sensitivity, led to the initial investigations of this material for treating tooth sensitivity. Research with NovaMin had shown that these materials will actually form a strong attraction with collagen.[17,18,26] Because dentin consists of collagen to a significant proportion, it was believed that the NovaMin particles would bind to the exposed dentin surface, as well as physically fill the open tubules. It was further hypothesized that the subsequent ionic release and surface reaction would help form a protective hydroxyl carbonate apatite layer that would impart rapid and continual relief from tooth sensitivity. The earliest studies conducted *in vitro* demonstrated that the material would, in fact, rapidly occlude dentin tubules and form a protective layer on the dentin surface.[27] These initial results were encouraging, and led to further research and the commercial development of this technology.

Role of pH and Ionic Release

To understand the details of the mechanisms of this action, it is necessary to review the combination of ionic reactions that occur in an aqueous environment, as well as other factors, such as pH changes and the surface changes in the particles themselves.

All have a critical role in producing the protective effect of this material.

It has been well established that when particles of NovaMin material are exposed to an aqueous environment such as water or saliva, there is an immediate release of sodium ions (Table I). The release of Na from the particle increases the local pH. This can cause a more rapid precipitation of the ions to form the HCA layer. It is well known that calcium phosphates are more soluble in acid environments than in basic or pH-neutral solutions,[28] and that precipitation of these ions is accelerated at neutral or basic pH levels. It is the release of Na and increase in pH that allows the conditions for the rapid precipitation of particles and the formation of the calcium phosphate layer.[5]

The immediate release of Na from the NovaMin particles is required to initiate the formation of the calcium phosphate layer. The rapid release of sodium allows the release of calcium and phosphate ions from the particles within minutes following exposure of NovaMin to the aqueous environment by forming a porous surface layer. The rate of release of these ions has been well established in many different models and, in fact, the earliest studies with these materials demonstrated that a calcium hydroxyapatite layer could be formed *in vitro*, even in the absence of an external source of calcium or phosphate.[1] An amorphous calcium phosphate layer was found to form on the particle surfaces within an hour of exposure to a simple organic buffer. It is important to realize that this unique attribute of the composition of calcium sodium phosphosilicate sets it apart from all other materials that have been shown to act as physical occluding materials. Further evidence to support this comes from numerous studies that have shown that the particles will act as reservoirs to continuously release calcium ions and phosphate ions into the local environment, over many days in some cases.[29]

In addition to the release of these ions, the role of soluble silica in the formation of calcium phosphate mineral has been established by various investigators. This is another factor that, in part, helps explain the mode of action of NovaMin in physically occluding tubules. Work performed by Damen and ten Cate in the late 1980s and early 1990s looked at the effect of soluble silica on precipitation of calcium phosphates.[29] In their work, they found that polymers of silicic acid promoted (increased the rate) the precipitation of hydroxyapatite, even in the presence of inhibitors of hydroxyapatite. These results are in agreement with a small, but ever increasing body of work that suggests that silica enhances the formation of hydroxyapatite in biological systems.[30] It is also an attribute of the NovaMin particles that they release silica into the environment (at a concentration between 15 and 40 ppm). This is thought to be one of the critical factors in the early stages of the precipitation of calcium phosphate. More recently, computer simulation of the interactions of small silica chains with calcium and phosphate ions has shown that a three-member silica chain is optimal as a nucleating site for hydroxyapatite formation.[31] These results support the proposed mechanism of bioactive glasses proposed by Hench and demonstrated in the action of NovaMin.

In order to be effective at occluding tubules, the particles must not only release ions at sufficient concentrations over time, but they must be able to remain on the dentin surface over a long period of time. The interactions of the NovaMin particles with collagen have been studied by a number of research groups in various *in vitro* models.[17,18] These studies have all demonstrated that there is a positive interaction between the reacted surface of the particles and collagen, and that this interaction is strongest for the composition used in NovaMin. These studies have shown that the development of the negative surface charge at the particle surface due to the initial reactivity allows for binding to the side groups on Type I collagen fibers. Because exposed dentin has a high content of exposed collagen, it is reasonable to assume that this is the mechanism that allows the NovaMin particles to attach to and remain on the dentin surface. Once deposited onto the dentin surface, the particles will continue to react and act as a reservoir for the continued long-term release of calcium and phosphate into the local environment.

Evidence of Efficacy for NovaMin

There are a number of established *in vitro* models in the area of oral healthcare that have been used to demonstrate the mode of action of the various desensitizing agents. The dentin block model has a number of variations to test the ability of materials to occlude tubules, and to remain on the dentin surface through various challenges that would normally be found in the oral environment. There has been extensive testing of NovaMin using a number of these models, and they have repeatedly demonstrated the rapid occlusion of tubules and the persistence of the particles on the dentin surface.[32] These studies have repeatedly shown that a single application of a sufficient concentration (above 3%) of NovaMin, either in a daily-use dentifrice or a professionally applied prophylaxis paste, is effective at blocking at least 75% of open tubules. In many cases, the single application is sufficient to block over 95% of tubules. Furthermore, these studies have demonstrated that a single application of NovaMin in these models will resist repeated acid challenges when tested in a model where the material is repeatedly applied and alternately subjected to twice-daily acid challenges; the results demonstrate continual blockage of the dentin tubules. Additional testing in these models has shown that NovaMin continues to release calcium ions over a long period of time compared with other calcium-containing products that release a burst of calcium, but then provide little in the way of calcium ions to protect the exposed dentin.

SEM is one of the most widely employed analytical techniques to evaluate the ability of dentifrice ingredients to occlude dentine tubules. Figure 2a is an SEM image that shows a typical prepared dentin block used in the types of *in vitro* studies described above. The piece of dentin has been ground and polished, and then acid-etched to remove the smear layer to provide a surface with patent tubules. Figure 2b shows a dentin block that has been treated once with the NovaMin material and subjected to a subsequent acid challenge. After the acid challenge, the sample was gently rinsed and dried for SEM analysis. Note that the majority of tubules are completely closed and the remainder are at least partially closed. Interestingly, there are particles that are retained on the surface of the dentin block even after rinsing. This evidence substantiates and helps to explain the long-lasting effect of even a single use of the NovaMin particles.

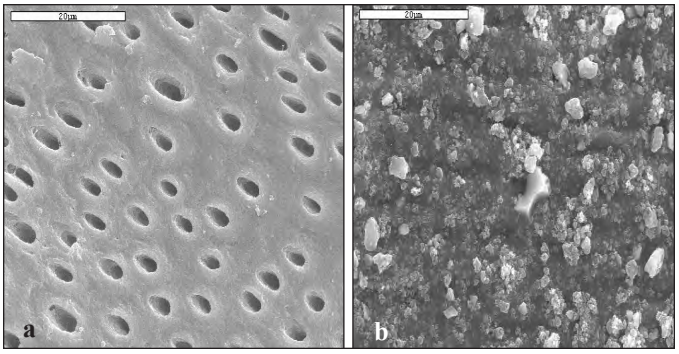


Figure 2. *a. Prepared dentin slab showing open tubules. b. Dentin after one application of NovaMin for two minutes and a 30-second water rinse.*

While *in vitro* studies are extremely useful in helping to differentiate rank and evaluate various materials for their effectiveness in treating tooth sensitivity, the clinical trial is the ultimate test for these materials. There have been a number of clinical studies performed with NovaMin. One study compared the efficacy of a strontium chloride dentifrice and a placebo to a daily-use NovaMin dentifrice in reducing tooth sensitivity in a six-week prospective study. The results showed that compared to placebo, both anti-sensitivity ingredients reduced sensitivity, but the NovaMin material showed statistically greater reductions in sensitivity at the six-week end point compared with the other materials.[33]

Commercialization of NovaMin for Treating Tooth Sensitivity

During the past 10 years, a number of consumer and professional products containing NovaMin have been introduced into the market. The first product developed by NovaMin Technology was Oravive®, a daily-use, fluoride-free dentifrice that contains 5% NovaMin. This product was cleared for use by the FDA through a 510(k) as a medical device for the rapid and continual reduction of tooth sensitivity through physical tubule occlusion. Other products that have been introduced are listed in Table II, along with their descriptions. Today, CSPS has been formulated into over 15 products and is sold in over 20 countries, including the US, Canada, India, China, and a number of countries in Europe. These products have proven to be effective and safe.[33-38]

Table II
A list of Some Currently Available NovaMin-Containing Products

Product	Description
SootheRx (US)	7.5% NovaMin, daily use, professionally supplied
X-Pur (Canada)	5.0% NovaMin, daily use
Nanosensitive (Germany)	7.5% NovaMin
Sensishield (UK)	5.0% NovaMin
Nutri-émail (France)	7.5% NovaMin
Vantaj	5.0% NovaMin
SHY-NM	5.0% NovaMin
Odontis Sensiblock (Brazil)	7.5% NovaMin

Development of new applications and refinements in the manufacture and use of NovaMin continues in the area of oral health care.[39] The interactions of the material with native collagen, along with the reactivity of the particles, ensures that the material will immediately occlude patent dentin tubules and will remain at the dentin surface, allowing this ionic release to build a thin mineral layer that will continue to occlude the tubules and will resist challenges of acidic environments.

The wealth of science behind the development of this class of materials has led to investigations of NovaMin for oral healthcare applications beyond the treatment of tooth sensitivity. The potential of these materials for remineralization of both enamel and dentin has been studied *in vitro* and *in situ* and holds promise.[40,41] In addition, the unique ionic reactions and potential antimicrobial and anti-inflammatory properties might prove useful in treating gingivitis.[42]

Acknowledgment: Publication of this review was supported by GlaxoSmithKline Consumer Healthcare.

For further correspondence with the author of this paper, contact Dr. David Greenspan—dspinode@gmail.com.

References

1. Hench LL, Andersson Ö. Bioactive glasses. In: *Introduction to Bioceramics*, Hench LL, Wilson J, eds., Singapore, World Scientific, pp. 41-62, 1993.
2. Hench L. Biomaterials. *Science* 1980;208:826-831.
3. Hench LL, Splinter RJ, Greenlee TK, Allen WC. Bonding mechanisms at the interface of ceramic prosthetic materials. *J Biomed Mater Res Symp* 1972;2:117-141.
4. Hench LL, Paschall HA. Direct chemical bond of bioactive glass-ceramic materials to bone and muscle. *J Biomed Mater Res* 1973;7:25-42.
5. Andersson OH, Kangasniemi I. Calcium phosphate formation at the surface of bioactive glass *in vitro*. *J Biomed Mater Res* 1991;25:1019-1030.
6. Clark AE, Pantano CG, Hench LL. Auger spectroscopic analysis of bioglass corrosion films. *J Am Ceram Soc* 1976;59:37-39.
7. Xynos ID, Hukkanen MV, Batten JJ, Buttery LD, Hench LL, Polak JM. Bioglass 45S5 stimulates osteoblast turnover and enhances bone formation *in vitro*: implications and applications for bone tissue engineering. *Calcif Tissue Int* 2000;67:321-329.
8. Day RM. Bioactive glass stimulates the secretion of angiogenic growth factors and angiogenesis *in vitro. Tissue Eng* 2005;11:768-777.
9. Xynos ID, Edgar AJ, Buttery LD, Hench LL, Polak JM. Ionic products of bioactive glass dissolution increase proliferation of human osteoblasts and induced insulin-like growth factor II mRNA expression and protein synthesis. *Biochem Biophys Res Commun* 2000;276:461-465.
10. Jones JR, Sepulveda P, Hench LL. Dose-dependent behavior of bioactive glass dissolution. *J Biomed Mater Res* 2001;58:720-726.
11. Oonishi H, Hench LL, Wilson J, Sugihara F, Tsuji E, Kushitani S, Iwaki H. Comparative bone growth behavior in granules of bioceramic materials of various sizes. *J Biomed Mater Res* 1999;44:31-43.
12. Cerruti MG, Greenspan D, Powers K. An analytical model for the dissolution of different particle size samples of bioglass in TRIS-buffered solution. *Biomaterials* 2005;26:4903-4911.
13. Arcos D, Greenspan DC, Vallet-Regí M. A new quantitative method to evaluate the *in vitro* bioactivity of melt and sol-gel-derived silicate glasses. *J Biomed Mater Res* 2003;65:344-351.
14. Stoor P, Söderling E, Salonen JL. Antimicrobial effects of a bioactive glass paste on oral microorganisms. *Acta Odontol Scand* 1998;56:161-165.
15. Allan I, Newman H, Wilson M. Antibacterial activity of particulate bioglass against supra and subgingival bacteria. *Biomaterials* 2001;22:1683-1687.
16. Rechtenwald JE, Minter RM, Rosenberg JJ, Gaines GC, Lee S, Moldawer LL. Bioglass attenuates a proinflammatory response in mouse peritoneal endotoxicosis. *Shock* 2002;17:135-138.
17. Zhong JP, LaTorre GP, Hench LL. The kinetics of bioactive ceramics Part VII: Binding of collagen to hydroxyapatite and bioactive glass. In: *Bioce-*

ramics 7, Andersson OH, Yli-Urpo A, eds., Proceedings of the 7th International Symposium on Ceramics in Medicine, Turku, Finland, July 1994.
18. Oréfice R, Hench LL, Brennan A. Evaluation of the interactions between collagen and the surface of a bioactive glass during *in vitro* test. *J Biomed Mater Res* 2009;90:114-120.
19. Brännström M, Aström A. The hydrodynamics of the dentine; its possible relationship to dentinal pain. *Int Dent J* 1972;22:219-227.
20. Absi EG, Addy M, Adams D. Dentine hypersensitivity. The development and evaluation of a replica technique to study sensitive and nonsensitive cervical dentine. *J Clin Periodontol* 1989;16:190-195.
21. Ishikawa S. [A clinico-histological study on the hypersensitivity of dentin.] *Kokubyo Gakkai Zasshi* 1969;36:278-298.
22. Schiff T, Bonta Y, Proskin HM, DeVizio W, Petrone M, Volpe AR. Desensitizing efficacy of a new dentifrice containing 5.0% potassium nitrate and 0.454% stannous fluoride. *Am J Dent* 2000;13:111-115.
23. Orchardson R, Gillam DG. Managing dentin hypersensitivity. *J Am Dent Assoc* 2006;137:990-998.
24. West NX, Hughes JA, Addy M. Dentine hypersensitivity: the effects of brushing toothpaste on etched and unetched dentine *in vitro*. *J Oral Rehabil* 2002;29:167-174.
25. Froum SJ, Weinberg MA, Tarnow D. Comparison of bioglass synthetic bone graft particles and open debridement in the treatment of human periodontal defects. A clinical study. *J Periodontol* 1998;69:698-709.
26. Efflandt SE, Magne P, Douglas WH, Francis LF. Interaction between bioactive glasses and human dentin. *J Mater Sci Mater Med* 2002;13:557-565.
27. Litkowski LJ, Hack GD, Sheaffer HB, Greenspan DC. Occlusion of dentin tubules by 45S5 bioglass. In: *Bioceramics 10*, Sedel L, Rey C, eds., Proceedings of the 10th International Symposium on Ceramics in Medicine, Paris, France, October, 1997.
28. LeGeros RZ, LeGeros JP. Dense hydroxyapatite. In: *An Introduction to Bioceramics* Hench LL, Wilson J, eds., World Scientific Publishing Company, Ltd., Singapore, pp. 139-180, 1993.
29. Damen JJ, ten Cate JM. Silica-induced precipitation of calcium phosphate in the presence of inhibitors of hydroxyapatite formation. *J Dent Res* 1992; 71:453–457.
30. Sarmento C, Luklinska ZB, Brown L, Anseau M, De Aza PN, De Aza S, Hughes FJ, McKay IJ. *In vitro* behavior of osteoblastic cells cultured in the presence of pseudowollastonite ceramic. *J Biomed Mater Res* 2004;69:351-358.
31. Sahai N, Anseau M. Cyclic silicate active site and steriochemical match for apatite nucleation on pseudowollastonite bioceramic-bone interfaces. *Biomaterials* 2005;26:5763-5770.
32. Burwell A, Jennings D, Muscle D, Greenspan DC. NovaMin and dentin hypersensitivity—*in vitro* evidence of efficacy. *J Clin Dent* 2010;21(Spec Iss):66-71.
33. Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J, Tai BJ. Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (novamin) for the treatment of dentin hypersensitivity. *Am J Dent* 2008;21:210-214.
34. Litkowski L, Greenspan DC. A clinical study of the effect of calcium sodium phosphosilicate on dentin hypersensitivity—Proof of principle. *J Clin Dent* 2010;21(Spec Iss):77-81.
35. Salian S, Thakur S, Kulkarni S, LaTorre G. A randomized controlled clinical study evaluating the efficacy of two desensitizing dentifrices. *J Clin Dent* 2010;21(Spec Iss):82-87.
36. Sharma N, Roy S, Kakar A, Greenspan DC, Scott R. A clinical study comparing oral formulations containing 7.5% calcium sodium phosphosilicate (NovaMin), 5% potassium nitrate, and 0.4% stannous fluoride for the management of dentin hypersensitivity. *J Clin Dent* 2010;21(Spec Iss):88-92.
37. Pradeep AR, Anuj SJ. Comparison of the clinical efficacy of a dentifrice containing calcium sodium phosphosilicate with a dentifrice containing potassium nitrate and a placebo on dentinal hypersensitivity: A randomized clinical trial. *J Periodontol* 2010;81:1167-1173.
38. Narongdej T, Sakoolnamarka R, Boonroung T. The effectiveness of a calcium sodium phosphosilicate desensitizer in reducing cervical dentin hypersensitivity: A pilot study. *J Am Dent Assoc* 2010;141:995-999.
39. Burwell AK, Litkowski LJ, Greenspan DC. Calcium sodium phosphosilicate (NovaMin): remineralization potential. *Adv Dent Res* 2009;21:35-39.
40. Alauddin SS, Greenspan DC, Anusavice KJ. *In vitro* human enamel remineralization using bioactive glass containing dentifrice. *J Dent Res* 2005; 84(Spec Iss A):2546.
41. Litkowski LJ, Quinlan KB, Pandya AJ. *In situ* comparison of surfaces by optical profilometry. *J Dent Res* 2007;86(Spec Iss A):1412.
42. Tai BJ, Bian Z, Jiang H, Greenspan DC, Zhong J, Clark AE, Du MQ. Antigingivitis effect of a dentifrice containing bioactive glass (novamin) particulate. *J Clin Periodontol* 2006;33:86-91.

NovaMin® and Dentin Hypersensitivity—*In Vitro* Evidence of Efficacy

Anora Burwell David Jennings Dave Muscle

NovaMin Technology Inc.
Alachua, FL, USA

David C. Greenspan, PhD

Spinode Consulting
Gainesville, FL, USA

Abstract

- **Objective:** The objective of this study was to determine the ability of a calcium sodium phosphosilicate (NovaMin®) particulate to occlude dentin tubules, and to characterize the nature of the occlusion through a number of *in vitro* studies.
- **Methods:** Four experiments were designed to demonstrate the ability of NovaMin to 1) rapidly occlude tubules, 2) remain on the dentin surface in the face of acid challenges, and 3) form a biologically stable hydroxycarbonate apatite layer on the surface of dentin. Bovine dentin samples, polished to 1200 grit silicon and etched in 40% w/w o-phosphoric acid solution for 15 minutes to remove the smear layer, were employed in all four experiments. Four different experimental techniques were used to evaluate the effects of NovaMin and other marketed calcium-based products on tubule occlusion in 1) a single-treatment model, 2) a 10-day acid challenge cycling model to evaluate tubule occlusion, 3) a 10-day acid challenge cycling model to evaluate changes in surface hardness, and 4) a calcium-release model. Samples were assessed for tubule occlusion by scanning electron microscopy, surface mineralization by microhardness, and calcium release by inductively coupled mass spectroscopy.
- **Results:** For the single-treatment model, statistical analysis showed that all treatment groups had statistically fewer open tubules than the control group (untreated; $p < 0.001$), and that the NovaMin group occluded significantly more tubules than the Quell® group ($p < 0.001$). For the cycling models, after a one-time brushing with the NovaMin (SootheRx™) dentifrice, significantly fewer open tubules were visible compared to the untreated control ($p < 0.001$). After the 10-day cycle, there were few visible open tubules on the samples treated with SootheRx, a significant reduction when compared to the control samples ($p < 0.001$). The hardness of dentin treated with NovaMin during the 10-day cycle was significantly greater than sound and demineralized dentin ($p < 0.001$). The calcium-release model demonstrated NovaMin-based dentifrices released less calcium initially compared to the other treatment groups. After four hours, a higher release of calcium was observed that was sustained over 24 hours.
- **Conclusion:** NovaMin adheres to an exposed dentin surface and reacts with it to form a mineralized layer. The layer formed is resistant to acid challenges and is mechanically strong. The continuous release of calcium over time is suggested to maintain the protective effects on dentin, and provide continual occlusion of the dentin tubules.

(J Clin Dent 2010;21[Spec Iss]:66–71)

Introduction

Dentin hypersensitivity is a common occurrence in the general adult population, and has been extensively studied and discussed.[1-6] Histological evaluation of dentin has shown that it contains numerous fluid-filled tubules that extend from the exterior surface to the pulp chamber. These tubules widen as they reach the pulp chamber. These observations led Gysi[7] to propose that the movement of fluid within these tubules away from the pulp stimulated the nerves associated with the odontoblasts at the pulpal end of the tubules, eliciting a pain response. Decades later, these observations led to the work of Brännström and the direct evidence for the hydrodynamic theory of dentin hypersensitivity,[8,9] and the consequence that by eliminating fluid flow in the tubule, the effects of dentin hypersensitivity can be reduced or eliminated. The hydrodynamic theory has been widely accepted and has been strengthened in recent years by excluding several other mechanisms, such as the innervations of the tubules and that odontoblasts might act as sensory receptors.[10]

There is a significant body of work that has refined the hydrodynamic theory in an attempt to find efficacious treatments for this condition. While it is known that the dentin tubules are not innervated by odontoblasts, it is also known that intradental nerves are directly stimulated by hydrodynamic action.[11,12] These studies showed that the outward flow of fluid evoked greater nerve activity than inward displacements. Other studies have shown that the condition of the dentin surface plays a large role in dentin sensitivity. It has been shown that sensitive dentin surfaces have patent tubules, and that non-sensitive surfaces have tubules that are filled with mineral.[10] It has also been shown that approximately 90% of hypersensitivity arises from the cervical margin on the buccal and, to a lesser degree, labial aspect of the tooth.[13] These data make the strong case that by eliminating fluid flow in the tubule, the effects of dentin hypersensitivity can be reduced or eliminated.

In recent years, a number of inorganic materials have been used in various dentifrice formulations with the goal of depositing material to physically occlude the tubules. Calcium sodium phosphosilicate (CSPS) is an inorganic amorphous material that was designed based on a class of materials known as bioactive glasses. This material has the trade name NovaMin® (NovaMin Technology Inc., Alachua, FL, USA), and is currently used in a number of daily-use and professionally dispensed products to

treat dentin hypersensitivity by physically occluding the dentin tubules. The material was originally developed as a bone regenerative material, and is part of a larger class of inorganic synthetic biomaterials known as bioactive ceramics. The unique aspect of this material is its ability to form a direct chemical bond with bone tissue, and to stimulate the repair process through a series of sequential, well-controlled surface reactions and ionic release.[14-16]

Studies have shown that ions released from the NovaMin, under a series of chemical reactions, will result in the formation of a carbonated hydroxyapatite layer on the surface of the material.[18] These reactions are sensitive to the particle size of NovaMin and the volume of solution to which the materials are exposed.[18,19] The reactions of the material result in significant levels of Ca and P released into solution, and these reactions result in an increase in solution pH. This slightly basic pH enhances the formation of the biologically relevant hydroxycarbonate apatite (HCA) on the material surface within a matter of hours. The ionic release from these materials and their ability to form a biologically equivalent carbonated hydroxyapatite led to investigations using fine particulates of CSPS for the treatment of dentin hypersensitivity. Initial *in vitro* studies demonstrated that a range of particle sizes could occlude dentin tubules *in vitro*.[20] These studies showed that not only did the particles block the tubules, but resulted in the potential formation of HCA on the surface of prepared dentin. This material has been incorporated into a number of daily-use dentifrice products as well as professionally applied products, and is sold in over 20 countries.

The objective of this work was to demonstrate the mechanisms of action of NovaMin through a number of *in vitro* studies, and to relate these results to the clinical success of this material.[21,22]

Materials and Methods

A series of similar *in vitro* tubule occlusion studies were designed to demonstrate the ability of NovaMin to rapidly occlude tubules, to remain on the dentin surface in the face of acid challenges, and to form a biologically stable mineral layer (HCA) on the surface of dentin as the result of long-term exposure to the fluids of the oral environment and against acid challenges.

The following studies were conducted:

1) A study comparing the efficacy of a one-time application of NovaMin to a commercial topical desensitizer (Quell® Desensitizer, Pentron Clinical Technologies, Wallingford, CT, USA) for the ability to occlude open tubules.
2) A study comparing the ability of a NovaMin-containing dentifrice (SootheRx™, NovaMin Technology Inc., Alachua, FL, USA) with a casein phosphopeptide-amorphous calcium phosphate topical cream (MI Paste) to occlude tubules in an *in vitro* remineralization/demineralization (remin/demin) model that would simulate typical acid challenges in the oral environment.
3) A study to investigate the surface layer formed by NovaMin in a 10-day acid challenge cycling model.
4) A study to investigate the ability of NovaMin to act as a continuous source of calcium over time.

Preparation of Bovine Dentin Samples

The root portion of bovine incisors was separated from the crown portion at the cemento-enamel junction (CEJ) using a diamond-embedded blade with a low-speed saw under irrigation. The root portions of the teeth were progressively ground at low speeds using 320, 600, and 1200 grit silicon carbide abrasive papers to expose and polish the dentin layer. Deionized (DI) water was kept flowing on the grinding surface during the procedure. The samples were rinsed three times in an ultrasonic bath using DI water for 15 minutes each rinse. Samples were then lightly etched in a 40% w/w o-phosphoric acid solution for 15 minutes to remove the smear layer. The samples were then immediately rinsed again for 15 minutes in DI water.

Preparation of Artificial Saliva

Artificial saliva was prepared to have the following composition: 2.200g/L gastric mucin, 0.38 g/L NaCl, 0.213 g/L $CaCl_2 \cdot H_2O$, 0.738 g/L $KPO_4 \cdot 3H_2O$, and 1.114 g/L KCL. The final pH was adjusted to 7.0 at 37˚C with 85% w/w lactic acid.

Remineralization/Demineralization Procedure

Following preparation of dentin, a remin/demin cycling procedure was performed in Studies II and III below. Briefly, samples were exposed to the demineralization solution for 30 minutes, removed from the solution, and brushed for two minutes with the appropriate test product, gently rinsed with DI water, then placed into the artificial saliva solution for eight hours. The samples were then placed into the demineralization solution again for 30 minutes, removed, and brushed with the appropriate product for two minutes followed by a gentle rinse. The samples were then placed back into the artificial saliva solution overnight. This constituted a one-day, two-acid challenge cycle.

Scanning Electron Microscopy (SEM) Analysis

At the end of each study, the teeth were dried at 37˚C and mounted for analysis using SEM. Teeth from each group in each study were mounted either on carbon disks and coated with carbon using a sputter coater, or on aluminum disks and coated with gold/palladium. The carbon coating allowed for energy dispersive x-ray analysis (EDXA) to determine the surface elemental composition of the dentin blocks, while the gold/palladium coating allowed for better image quality and quantitative analysis of the open and closed tubules. SEM images were captured at 500× and 2000× magnification from three randomly chosen spots on each dentin surface for analysis. An SEM technician not associated with the project team randomly focused on a spot on each sample. From this starting point, the random spots were chosen by moving the x-y stage the same distance from the starting point for each spot, thus ensuring no bias was introduced by the person taking the images.

Quantitative Evaluation of Tubule Occlusion

Tubule counting was performed on all SEM images that were obtained at 2000× (15 images per treatment group, except where noted below). An independent SEM technician was told to find a starting location, and then move the x and y axes by a set distance. That distance was used to capture an image. He then

continued to move the sample in both the x and y directions by that same distance. In this way, unbiased regions of each sample were collected. Three examiners, blinded to the treatments, each counted the number of open tubules and partially open tubules. Tubules that could not be fully visualized on the SEM images were not counted. For each SEM image, the tubule counts from the three persons were averaged together to obtain the number of open and partially occluded tubules. For each treatment group, the data from the 15 SEM images were averaged together and statistically analyzed using Sigma Plot software.

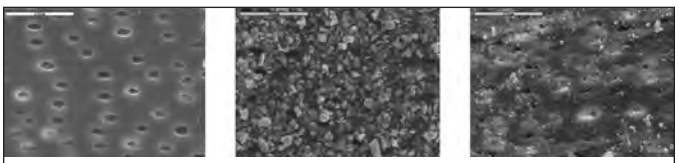
Evaluation of Surface Microhardness

The microhardness was measured with a Knoop indenter on a MicroMet 5101 Hardness Tester (Buehler Ltd., Lake Bluff, IL, USA). Microhardness was measured with a load of 50–100 grams and a dwell time of 20 seconds. The dimensions of all indentations were measured immediately following indentation with OmniMet imaging software (Buehler, Ltd.) to avoid possible shrinkage caused by mechanical recovery of the tooth surface.

Results

Study I

This study compared the efficacy of a one-time application of NovaMin to a commercial topical desensitizer (Quell Desensitizer) for the ability to occlude open tubules. Quell Desensitizer is a two-part system that results in the precipitation of an inorganic phosphate that is claimed by the manufacturers to occlude dentin tubules. Bovine dentin was prepared as described above. Twenty-five dentin slabs each were used for the NovaMin material and the Quell Desensitizer. Twenty-four prepared dentin blocks served as negative controls. The average particle size of the NovaMin material was five microns in this study. The NovaMin material was mixed with water using a 1:3 wt/vol ratio, applied as a slurry to the dentin surface, and allowed to remain for one minute before undergoing a gentle 15-second water rinse. The Quell Desensitizer was used according to the manufacturer's instructions. This procedure consisted of applying a Ca-containing solution with a swab to the dentin surface, allowing it to remain undisturbed for 30 seconds, and then applying a second phosphate-containing solution. Following treatment, the specimens were air dried and prepared for analysis by SEM and Energy Dispersive Spectroscopy (EDS). From the SEM images at 2000× magnification, the number of fully open tubules and partially open tubules were manually counted and summed, and ANOVA and pair-wise comparisons were conducted using a Bonferroni p-value criterion ($p = 0.05/3 = 0.0167$) to evaluate and compare the treatment methods. Figure 1 shows representative images of the three groups tested.



a. Negative Control (untreated) **b.** Test Group (NovaMin) **c.** Positive Control (Quell)

Figure 1. *Representative SEM images of dentin following treatment. All images are at 200× magnification.*

Table I presents the mean number of open tubules as a function of treatment group.

Table I
Descriptive Statistics for Tubule Count

Treatment Group	Number of Samples	Open Tubule Count (Mean)	Standard Deviation	Standard Error
Negative Control (untreated)	24	37.79	20.58	4.20
Test (NovaMin)	25	6.96	11.01	2.20
Positive Control (Quell)	25	26.00	21.65	4.33

As stated in the Materials and Methods section, 15 images per group were analyzed and three dentin samples per group were evaluated. The mean number of open tubules in the control group was 37.79. The mean number of open tubules for the NovaMin-treated group was 6.96, while the Quell group averaged 26.00. The statistical analysis showed that both treatment groups had statistically fewer open tubules than the control group ($p < 0.001$), and that the NovaMin group occluded significantly more tubules than the Quell group ($p < 0.001$). In addition, EDS analysis demonstrated a significant calcium phosphate layer with the presence of silica in the NovaMin-containing group (data not shown).

Study II

The purpose of this work was to compare the ability of a NovaMin-containing dentifrice (SootheRx) with a casein phosphopeptide-amorphous calcium phosphate topical cream (MI Paste™, GC America Inc., Alsip, IL, USA) to occlude dentin tubules in an *in vitro* remin/demin model that would simulate typical acid challenges in the oral environment. One group of dentin samples (n = 5 for each group) was brushed once for two minutes with either the NovaMin-containing SootheRx dentifrice, Recaldent™-containing MI Paste, or DI water (control group). The samples were then gently rinsed with water for 15 seconds, dried, and used for SEM analysis. A second group of samples was subjected to a 10-day remin/demin cycle (a total of 20 treatments) that consisted of a twice-daily 30-minute soak in demineralizing solution as described above, followed each time by a two-minute brushing with either SootheRx, MI Paste, or DI water. Samples were soaked in an artificial saliva solution as described above at 37˚C between the two daily demineralization/brushing periods. Quantitative tubule occlusion data were obtained from scanning electron microscopy (SEM) images of the treated samples taken at a magnification of 2000×. Data were statistically analyzed using SigmaPlot software (v9.01, Systat Software, Inc., Chicago, IL, USA). Data did not have a normal distribution so the nonparametric ANOVA on Ranks test was used to detect significance. When significance was detected, pair-wise comparisons were made using the nonparametric Dunn's test (significant if $p < 0.01$). Data are reported as mean ± standard error of the mean.

The results of the tubule occlusion data are shown in Figure 2. After a one-time brushing with the SootheRx dentifrice, significantly fewer open tubules (12.2 ± 1.6) were visible in an SEM image compared to the control samples (62.3 ± 7.0, $p < 0.001$). The number of open tubules on samples brushed once with MI

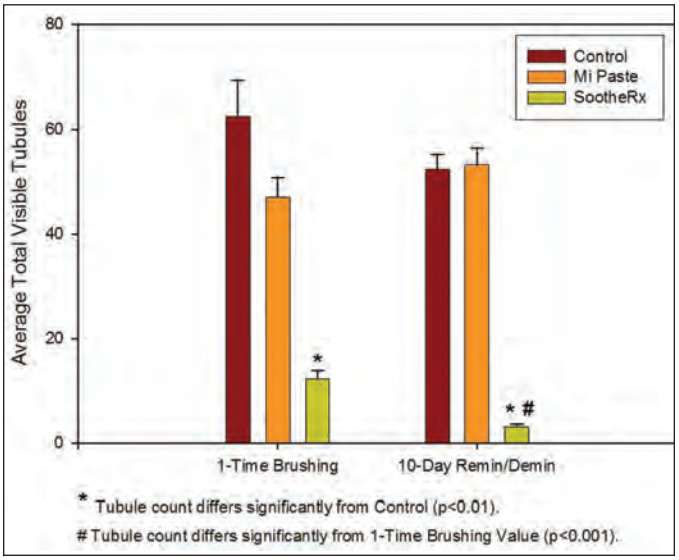


Figure 2. *Comparison of tubule occlusion between treatments at one-time brushing and 10-day re/demineralization time points.*

Paste (47.1 ± 3.7) did not differ significantly from the control samples. After the ten-day remin/demin cycle, there were few visible open tubules on the samples treated with SootheRx (3.1 ± 0.4); a significant reduction when compared to the control samples (52.4 ± 2.9, $p < 0.001$). Treatment with MI Paste did not significantly reduce the number of open tubules (53.2 ± 3.1) compared to the control samples. Figure 3 shows representative SEM images of the prepared dentin surface, a one-time brushing

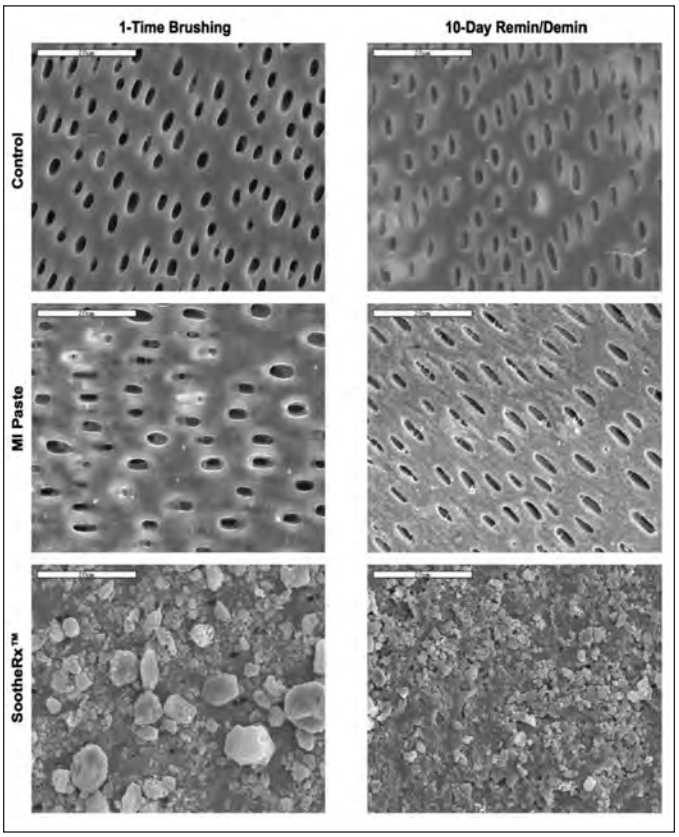


Figure 3. *Scanning electron micrograph of one-time and 10-day remin/demin study.*

with each material, and the surfaces after 10-day brushing and acid challenge. It is clear from viewing these images that not only has there been significant deposition of particles of NovaMin, but there appears to be a film covering the dentin in between particles. This change in surface morphology between the control surface which appears to be smooth and even, and the treated surfaces is observed in all samples.

Study III

The purpose of this study was to investigate the surface layer formed from the NovaMin in a 10-day acid challenge cycling study. Bovine tooth roots were ground, polished, and acid-etched to expose the dentin layer and create an *in vitro* hypersensitivity model using the methods described above. Randomly selected samples were left untreated and represent "sound" dentin. The remaining samples were subjected to a ten-day acid challenge/artificial saliva cycle that consisted of a twice-daily 30-minute soak in demineralizing solution (pH = 4.52) at 37˚C, followed by a two-minute brushing with either NovaMin-containing SootheRx, Recaldent-containing MI Paste, or DI water. Samples were soaked in artificial saliva (pH = 7.00) at 37˚C between the two daily demineralization/brushing periods. Samples treated with only DI water are referred to as "demineralized" dentin. Knoop hardness (KH) was measured on all dentin surfaces using a load of 50 grams for 15 seconds. Results were analyzed using ANOVA and Holm-Sidak tests ($p < 0.01$).

Figure 4 shows the results of the Knoop hardness data. All data are presented as mean ± SE, with n = 15 for each group. Demineralized dentin had a KH (50.85 ± 0.85) that was significantly lower than sound dentin (65.43 ± 0.50, $p < 0.001$). The KH of dentin treated with NovaMin during the remin/demin cycle (79.75 ± 1.10, $p < 0.001$) was significantly greater than sound and demineralized dentin. Dentin treated with Recaldent had a KH (52.12 ± 1.27) that was significantly lower than sound dentin ($p < 0.001$) and did not differ from demineralized dentin ($p = 0.358$).

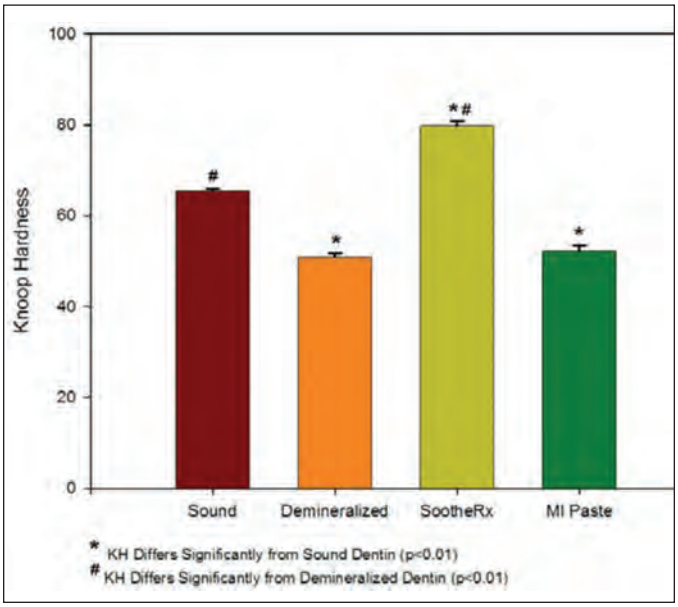


Figure 4. *Surface microhardness for each treatment group.*

Study IV

The objective of this study was to investigate the ability of different products to act as a continuous source of calcium over time. The products tested were; MI Paste (10% CPP-ACP, Recaldent), Oravive® (5% NovaMin, NovaMin Technology Inc., Alachua, FL, USA), and SootheRx (7.5% NovaMin). Dilutions of dentifrice in DI water (1:200) were mixed thoroughly using a laboratory vortexer and placed in an incubator shaker at 37˚C and 275 rpm. After one, four, and 24 hours, the samples were centrifuged, supernatants were decanted, and the samples were re-suspended in fresh DI water. The recovered supernatants were analyzed for calcium ion content using inductively coupled plasma (ICP) spectroscopy, and pH changes using an Ag/AgCl electrode. Three different samples were used at each time point, and three independent measures at each time point were taken and averaged. Data were statistically analyzed by comparing Ca release within each group using ANOVA and Holm-Sidak methods, with $p < 0.01$ ($n = 3$). Values with the same superscript were not significantly different ($p < 0.01$, Table II).

Table II
Changes in Ca Concentration and pH as a Function of Time for the Products Tested

Test Products	Calcium Concentration (μg[Ca^{2+}]/g Dentifrice ± SEM)			Solution pH (Mean ± SEM)		
	1 Hour	4 Hour	24 Hour	1 Hour	4 Hour	24 Hour
MI Paste	12937 ± 89	371 ± 5	121 ± 6	8.13 ± 0.06	7.13 ± 0.11	5.59 ± 0.22
Oravive	1522 ± 50	3050 ± 42	2961 ± 38	9.40 ± 0.00	9.38 ± 0.02	9.30 ± 0.02
SootheRx	2645 ± 30	3993 ± 24	3956 ± 35	9.51 ± 0.02	9.59 ± 0.00	9.68 ± 0.00

The CPP-ACP dentifrice released a large burst of calcium within one hour (12937 ppm) which was significantly greater ($p < 0.001$) at one hour than at four hours or 24 hours ($p < 0.001$). The pH of the CPP-ACP paste was also significantly different at one hour compared with four hours ($p = 0.03$), as well as one hour compared with 24 hours ($p < 0.001$) and four hours versus 24 hours ($p < 0.001$). For the Oravive group, the Ca release was significantly greater at four hours ($p < 0.001$) and at 24 hours ($p < 0.001$) compared with the one-hour release. The pH was not significantly different at any time point. The release of Ca from the SootheRx group was significantly greater at four hours and 24 hours compared with the one-hour release ($p < 0.001$), but there was no statistically significant difference in the release at four hours compared with 24 hours ($p = 0.379$). There was no statistically significant difference in pH of the SootheRx group at any time point. NovaMin dentifrices released less calcium initially when compared to the CPP-ACP group, but increased by four hours and sustained significant release through 24 hours. The NovaMin-containing products also elevated and maintained solution pH at all time points.

Discussion

Dentin hypersensitivity is a very common occurrence in the adult population worldwide. The basic description of the condition advanced by Gysi, and the acceptance of the hydrodynamic theory of Brännström, has resulted in two basic approaches to treat dentin hypersensitivity; either by depolarizing the nerves through chemical means or attempting to physically occlude the dentin tubules. The series of *in vitro* studies reported in this article were conducted to demonstrate the properties and mechanism of action of a unique class of bioactive material, calcium sodium phosphosilicate, for the treatment of dentin hypersensitivity by the occlusion of dentin tubules. The premise is that the reactivity of the particles allows for a change in surface charge and structure that causes the particles to adhere to the dentin surface, especially the open tubules. At the dentin surface, NovaMin reacts with the saliva and releases ions to form a mineral layer on the surface of the dentin that appears very similar to a biological apatite.

The results shown in Table I, using a one-time application of the calcium sodium phosphosilicate particles followed by a water rinse, demonstrate that this material has an affinity for the dentin surface. Previous studies have shown that there is a strong bond that develops when NovaMin (CSPS) comes in contact with collagen.[23,24] The surface charge that develops as a result of the ionic activity allows bonding to specific side chains on the collagen molecule. The SEM images shown in Figure 1 clearly show that even after a 15-second water rinse, the surface is essentially covered by NovaMin particles.

The initial deposition of NovaMin onto a dentin surface and the ability to occlude the tubules is apparent. However, this demonstration is not sufficient to establish the efficacy of NovaMin in maintaining long-term tubule occlusion. Normal challenges to the oral environment, such as acidic liquids, mastication, and normal salivary flow are likely to remove the particles at the surface if they are not chemically bound in some manner to the tooth structure. The results shown in Figure 2 clearly demonstrate that NovaMin not only immediately binds to the dentin surface, but that over time it remains on the surface and continues to occlude the dentin tubules even after acid challenges. The SEM images in Figure 3 confirm these results. The observation that there is also a film-like structure that is formed on the dentin surface after treatment with NovaMin is consistent with the proposed mode of action for the formation of an HCA layer that is the result of the ionic release from the particles, as described by Hench and Paschall.[15] This is clear after only one treatment and is also observed after a 10-day cycle. This can be explained by understanding the mechanisms of the ionic release. When the particles are first subjected to the oral environment, sodium ions are released and this results in a large increase in the surface area of the particles.[25] In addition, there is a slight increase in the pH around the particles. The initial reactions then allow calcium to be released from the particles along with small amounts of phosphate. The local increase in pH helps to initiate the precipitation of calcium phosphate onto the surface.[19,26,27] The SEM images in Figure 3 show evidence of the changes that occur with this material as a result of continued exposure to a simulated saliva environment and the repeated acid challenges. Notice that while the tubules in both one-day and ten-day images are completely occluded, one can see some larger particles after just one brushing, whereas there are only smaller particles visible after ten days. This is possibly due to the fact that the reaction sequence consumes much of the particle as the ions are released. It is also a possibility that only the larger particles will be resident

on the surface for a long duration. In either case, these results demonstrate that NovaMin is not nearly as affected by acid challenge as is an amorphous calcium phosphate material, which is much more soluble in acidic environments.

The evidence of the formation of the HCA layer that imparts a long-term occlusive layer is demonstrated by the microhardness data shown in Figure 4. After a 10-day study where twice-daily brushing was followed by acid challenges, the microhardness of NovaMin-treated dentin slabs was significantly higher than the acid-challenged dentin or the dentin treated with the amorphous calcium phosphate material. In fact, the dentin slabs treated with NovaMin were harder than the control dentin. This can partially be explained by the fact that the surfaces were covered with NovaMin and this likely added to the resistance of the micro-indenter. It is also likely that the formation of the continuous HCA layer added to the mechanical strength of the surface layer and protected the dentin from demineralization. The data in Table II also demonstrate that the continued release of calcium ions over time helps to produce the protective film on the surface of the dentin. It is this series of reactions over time that produces the continuous layer considered to be HCA, that occludes the dentin tubules.

Conclusions

This series of *in vitro* studies has demonstrated that NovaMin will immediately be attracted to an exposed dentin surface, and that the material will begin to react with that surface, according to the established mechanism,[5] to form an HCA layer. Furthermore, these *in vitro* studies have shown that the layer formed is resistant to acid challenges and is mechanically strong. The continuous release of Ca over time helps to maintain the protective effects on dentin, and provides for continual occlusion of the dentin tubules. Further clinical research is needed to demonstrate that this mode of action carries over to the clinical relief of dentin hypersensitivity.

Acknowledgment: This work was funded by NovaMin Technology Inc. The authors would also like to acknowledge Kevin McKenzie for his work on the laboratory studies and Wayne Acree of the Major Analytical Instrumentation Center at the University of Florida for his work on the SEM analysis. Publication of this review was supported by GlaxoSmithKline Consumer Healthcare.

For further correspondence with the authors of this paper, please contact Dr. David C. Greenspan—dspinode@gmail.com.

References

1. Rees JS, Addy M. A cross-sectional study of dentine hypersensitivity. *J Clin Periodontol* 2002;29:997-1003.
2. Irwin CR, McClusker P. Prevalence of dentine hypersensitivity in a general dental population. *J Ir Dent Assoc* 1997;43:7-9.
3. Chabanski MB, Gillam DG, Bulman JS, Newman HN. Prevalence of cervical dentine sensitivity in a population of patients referred to a specialist periodontology department. *J Clin Periodontol* 1996;23:989-992.
4. Canadian Advisory Board on Dentin Hypersensitivity. Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. *J Can Dent Assoc* 2003;69:221-226.
5. Orchardson R, Collins WJ. Clinical features of hypersensitive teeth. *Br Dent J* 1987;162:253-256.
6. Dowell P, Addy M. Dentine hypersensitivity – a review. Aetiology, symptoms and theories of pain production. *J Clin Periodontol* 1983;10:341-350.
7. Gysi A. An attempt to explain the sensitiveness of dentine. *Br J Dent Sci* 1900;43:865-868.
8. Brännström M, Lindén LA, Johnson G. Movement of dentinal and pulpal fluid caused by clinical procedures. *J Dent Res* 1968;47:679-682.
9. Brännström M. The hydrodynamic theory of dental pain: sensation in preparations, caries, and the dentinal crack syndrome. *J Endod* 1986;12:543-457.
10. Markowitz K, Pashley DH. Discovering new treatments for sensitive teeth: the long path from biology to therapy. *J Oral Rehabil* 2007;35:300-315.
11. Andrew D, Matthews B. Displacement of the contents of dentinal tubules and sensory transduction in intradental nerves of the cat. *J Physiol* 2000;529:791-802.
12. Matthews B, Vongsavan N. Interactions between neural and hydrodynamic mechanisms in dentine and pulp. *Arch Oral Biol* 1994;39(Suppl):87s-95s.
13. Orchardson R, Collins WJ. Clinical features of hypersensitive teeth. *Br Dent J* 1987;162:253-256.
14. Hench LL, Polak JM. Third generation biomaterials. *Science* 2002;295:1014-1017.
15. Hench LL, Paschall HA. Direct chemical bonding between bio-active glass-ceramic materials and bone. *J Biomed Maters Res* 1973;7:25-42.
16. Ogino M, Ohuchi F, Hench LL. Compositional dependence of the formation of calcium phosphate films on bioglass. *J Biomed Mater Res* 1980;14:55-64.
17. Rehman I, Smith R, Hench LL, Bonfield W. FT-Raman Spectroscopic analysis of natural bones and their comparison with bioactive glasses and hydroxyapatite. In: *Bioceramics 7,* Andersson ÖH, Yli-Urpo A, eds., Butterworth-Heinemann Ltd., Oxford, England, pp. 79-84, 1994.
18. Arcos D, Greenspan DC, Vallet-Regí M. A new quantitative method to evaluate the *in vitro* bioactivity of melt and sol-gel derived silicate glasses. *J Biomed Mater Res* 2003;65:344-351.
19. Cerruti MG, Greenspan D, Powers K. An analytical model for the dissolution of different particle size samples of bioglass in TRIS-buffered solution. *Biomaterials* 2005;26:4903-4911.
20. Litkowski LJ, Hack GD, Sheaffer HB, Greenspan DC. Occlusion of dentin tubules by 45s5 bioglass. In: *Bioceramics 10, Proceedings of the 10th International Symposium on Ceramics in Medicine, Paris, France*, L. Sedel L, Rey C, eds.
21. Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J, Tai BJ. Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (NovaMin) for the treatment of dentin hypersensitivity. *Am J Dent* 2008;21:210-214.
22. Litkowski LJ, Quinlan KB, Pandya AJ. *In situ* comparison of surfaces by optical profilometry. *J Dent Res* 2007;86(Spec Iss A):1412.
23. Oréfice R, Hench L, Brennan A. Evaluation of the interaction of collagen and the surface of a bioactive glass during *in vitro* test. *J Biomed Mater Res* 2009;90:114-120.
24. Efflandt SE, Magne P, Douglas WH, Francis LF. Interaction between bioactive glasses and human dentin. *J Mater Sci Mater Med* 2002;13:557-565.
25. Hench LL, Andersson Ö. Bioactive glasses. In: *Introduction to Bioceramics*, Hench LL, Wilson J, eds., Singapore, World Scientific, pp. 41-62, 1993.
26. Burwell AK, Greenspan DC. Quantitative tubule occlusion in an *in vitro* remineralization/ demineralization model. *J Dent Res* 2006;85(Spec Iss C):568.
27, Burwell AK, Greenspan DC. Potential for dentifrice protection against enamel erosion in an *in vitro* model. *Caries Res* 2007;41:295-330.

The Role of Ionic Release from NovaMin® (Calcium Sodium Phosphosilicate) in Tubule Occlusion: An Exploratory *In Vitro* Study Using Radio-Labeled Isotopes

Guy LaTorre

NovaMin Technology Inc.
Alachua, FL, USA

David C. Greenspan, PhD

Spinode Consulting
Gainesville, FL, USA

Abstract

- **Objective:** The primary objective of this work was to develop a method of quantifying the levels and source of calcium and phosphate deposited on dental hard tissue from a novel calcium phosphosilicate (NovaMin®) material using neutron activation analysis (NAA). A second objective was to explore the utility of radiotracing to determine dentin porosity following exposure to calcium phosphosilicate.
- **Methods:** Neutron activation was used to create isotopes of Ca and P in the calcium phosphosilicate particles. Gamma radiation emitted from these isotopes was used to identify and measure their uptake (concentration) onto dental hard tissue. Three experiments were conducted to explore calcium and phosphate uptake to dental hard tissue: 1) a dose response to quantify the relative levels of calcium and phosphate deposited on dental hard tissue as a function of calcium phosphosilicate dose; 2) the effect of calcium phosphosilicate particle size on the relative levels of calcium and phosphate uptake; and 3) the permeability of calcium phosphosilicate-treated dentin by employing the radiotracer technetium. For all experiments, extracted bovine incisors were employed as the test substrate.
- **Results:** The results indicate there is a strong dose relationship between the wt% and particle size of calcium phosphosilicate in the dentifrice formulation and new Ca and P deposition. At above 5.0 wt% calcium phosphosilicate, there appears to be an exponential increase in the number of counts from the tooth surface. Finer particle size calcium phosphosilicate appears to deposit much higher levels of Ca and P than the larger range of particle sizes. The results from the technetium study show that when treated with the dentifrice slurry containing calcium phosphosilicate, dentin shows only a slight amount of technetium infiltration, indicating a lowering of dentin permeability.
- **Conclusion:** This exploratory study has demonstrated that NAA and the use of radio isotopes have utility in monitoring the uptake of Ca and P into both dentin and enamel tooth structure. The data generated from these studies have shown that there is a dose dependence and particle size effect for calcium phosphosilicate on the deposition of calcium and phosphate to dental hard tissue.

(J Clin Dent 2010;21[Spec Iss]:72–76)

Introduction

The diagnosis and treatment of dentin hypersensitivity (DH) has been the subject of intense investigations for over 100 years.[1] The diagnosis of DH in a clinical setting is often difficult, as the condition is not always isolated and can be caused by a number of other problems, including cracked or chipped teeth, leaky margins around restorations, caries, and gingival recession associated with age or periodontal disease.[2] The diagnosis of the problem is also confounded by the fact that patients often underreport the condition, as they feel it is not a significant enough problem that is worthy of mentioning to their busy dentist or hygienist.[3]

It is generally agreed that the cause of DH is associated with the movement of fluids within the dentinal tubules, as described by the Hydrodynamic Theory based on the work of Brännström.[4] Briefly, external stimuli, including thermal, evaporative, tactile, osmotic, or chemical, cause fluid movement within the dentinal tubules that results in stimulation of the nerve fibers causing pain. These stimuli most often come in the form of hot or cold foods, sweets and sugary beverages, and can also be experienced by the sensitive patient during routine dental examinations and cleanings.

A number of in-office and at-home treatment approaches for DH have been used in an attempt to successfully manage the condition.[5] While many different materials and approaches have been tried by clinicians to treat DH, most treatments fall into two categories, nerve desensitizers and tubule-occluding agents, which act to physically block open dentin tubules.

Early work conducted by Hodosh identified potassium nitrate as a superior desensitizer, and this resulted in the introduction of this potassium salt in a commercial dentifrice.[6] The mechanism of action of potassium nitrate is related to the ability of the potassium ion to depolarize the nerve and prevent the conduction of a pain signal. Early experiments conducted by Markowitz and Kim identified the potassium ion as the active component in a variety of potassium salts, including potassium nitrate.[7,8] It is believed that increasing the concentration of potassium ions in the fluids surrounding the nerve depolarizes the nerve, making it unresponsive to the stimuli that can cause pain.[8] The use of

potassium nitrate desensitizers has expanded beyond commercial dentifrices, and the ingredient is used in a number of professional dental applications

Physically blocking the dentin tubule can reduce the movement of fluid toward the pulp chamber and reduce the associated stimulation of the nerve fibers. Over the years, there have been many tubule occluding agents developed for both in-office and at-home treatment of exposed dentin. The most popular product form for in-office treatments is paint-on products that are based on oxalates, glutaraldehydes, or resins.[9] Products for at-home use typically employ potassium salts, strontium, or stannous salts.[10]

More recently, approaches in the treatment of DH are employing the use of calcium phosphate technologies which form precipitates to occlude dentinal tubules.[11] These technologies are based on their potential to remineralize tooth structure by-increasing salivary calcium and phosphate levels and, in some cases, increasing the saliva pH, resulting in the formation of calcium phosphate or hydroxyapatite.[12] One of these technologies is based on a bioactive glass composition that was originally developed to regenerate bone, and then adapted to incorporate into a broad range of oral care products (NovaMin®, NovaMin Technology Inc., Alachua, FL,USA).

NovaMin is a particulate bioactive glass composition that is composed of oxides of calcium, sodium, phosphorous, and silica (chemical name, calcium sodium phosphosilicate). Previous studies have shown that when the NovaMin composition comes in contact with simple biological solutions, the material rapidly releases calcium, sodium, and phosphorous ions which results in the formation of hydroxycarbonate apatite (HCA) that is similar in composition to the mineral found in both teeth and bones.[13,14] These early studies in simple biological solutions like tris buffer or simulated body fluid were early indicators of NovaMin's reactivity in aqueous environments.

To successfully develop an optimized and efficacious dentifrice formulation, the amount or dose of NovaMin within the formulation that is required to effectively remineralize tooth structure needs to be determined. In addition, the reactivity of NovaMin in the presence of typical dentifrice ingredients needs to be established. However, there is a significant experimental challenge in being able to quantify calcium and phosphate uptake to a substrate already rich in calcium and phosphate. To explore these fundamental questions, a series of experiments was conducted by South West Research Institute (SWRI, San Antonio, TX, USA) employing a technique called "neutron activation." Using this technique, the aim of this study was to demonstrate that it is possible to differentiate the calcium and phosphate deposited on dental tissue through the dentifrice, from the calcium and phosphate that is intrinsic to dental tissue.

Briefly, neutron activation analysis (NAA) is a nuclear method of determining the concentrations of elements in a wide variety of materials.[15] The sample is first placed in a neutron flux reactor where it undergoes bombardment with neutrons to create radioactive isotopes that can be identified; the element concentrations are determined by the gamma rays emitted from the material using scintillation counting.

The objective of this work was to use neutron activation for the first time in order to 1) determine the relative levels of calcium and phosphate deposited on dental hard tissue as a function of NovaMin formulation dose, 2) study the effect of particle size on the relative levels of calcium and phosphate uptake, and 3) explore the permeability of NovaMin-treated dentin by employing the radiotracer technetium. Due to the exploratory nature of these studies and the availability of an accessible neutron source, it was not possible to conduct these experiments with a replicate number suitable to provide meaningful statistics. Nonetheless, this study provides important results and methodology that can encourage scientific debate.

Materials and Methods

Preparation of NovaMin Particulate

A range of NovaMin particles was used in these studies. The materials were obtained from NovaMin Technology Inc. Particle size ranges included 15 μm to 1 μm, 90 μm–1 μm, and 90 μm-38 μm. These materials were obtained following standard manufacturing production processes.

Preparation of NovaMin Isotopes

Neutron activation was used to create isotopes of Ca and P in the NovaMin particles in order to determine the concentrations of these elements in Experiments 1 and 2. The samples were placed in a neutron flux reactor and bombarded with neutrons to create radioactive isotopes ^{45}Ca and ^{32}P. These isotopes emit gamma radiation which was subsequently used to measure their concentration in the studies. The isotopes ^{45}Ca and ^{32}P have half lives of 165.0 days and 14.3 days, respectively, allowing ample time to measure the tooth surface after treatment without losing the isotope concentration through decay. In Experiment 3, a metastable isotope of technetium, ^{99m}Tc, was obtained through neutron activation.

Preparation of Tooth Surfaces

For the first two experiments, extracted bovine incisors were prepared by first cutting off the tooth root just above the cementoenamel junction (CEJ) using a diamond saw, and then removing the tooth pulp. Once the tooth roots had been removed, the bottom of the each tooth, including the pulp cavity, was impregnated with a five-minute, curable, two-part epoxy resin which was allowed to cure for one hour.

For the third experiment (technetium 99 [m] study), extracted bovine incisors were prepared by first cutting off the tooth root several millimeters below the CEJ using a diamond saw, and then removing the tooth pulp. Once the tooth roots and pulp were removed, a stainless steel tube was inserted into the remaining root, taking care not to enter the pulp cavity, and the tube was then cemented into place using a five-minute, curable, two-part epoxy resin which was allowed to cure for one hour. The tube was used to provide a means of pressurizing and evacuating the pulp cavity. The evacuation created a positive pressure gradient from the tooth surface inward, which enhanced the infiltration of the solutions used in the experiment. The labial surface of each incisor was then ground and polished using a series of silicon carbide papers while under a flow of deionized (DI) water. After polishing, the samples were then lightly etched using a 5% phosphoric acid solution for five minutes, and then sonicated in DI water to remove

any residual smear layer. This process created open tubules from the dentin surface into the pulp chamber.

Experiment 1—Dose Effects

To explore a dose effect on the relative levels of calcium and phosphate deposited on the tooth section, neutron-activated NovaMin material was mixed into a commercially available dentifrice formulation at concentrations of 0.01%, 0.05%, 0.1%, 0.5%, 1.0%, 5.0%, 7.5%, and 10.0% NovaMin by weight. For this experiment, NovaMin particles with a size range of 90 µm-1µm were used. After preparation, the teeth were then treated with a 1:1 mixture of each dentifrice formula and DI water by two consecutive three-minute applications using a cotton-tipped swab, with a one-minute rinse with DI water between applications. Teeth were then dried to remove any excess liquid and placed into a 10 ml vial of Ready Gel™ (Bio-Rad Co., Hercules, CA, USA) liquid scintillation cocktail, with the treated surface facing the top of the standard scintillation vial. Measurements were taken using a Beckman Instruments LS 6000 TA Scintillation Counter, and scintillation counts were used to quantify new Ca and P deposited on the surface.

Experiment 2—Particle Size

To explore the effect of particle size on the relative levels of calcium and phosphate on the tooth section, neutron-activated NovaMin material, with three different particle size distributions, were tested in a 1:1 slurry of DI water and a NovaMin dentifrice at a 7.5% concentration. This concentration was chosen from the results of the first experiment. The particle size ranges tested included a small particle size range (15 µm-1 µm), a broader range of NovaMin particulate (90 µm-1 µm), and a larger particle size fraction (90 µm-38 µm). Extracted bovine incisors were prepared as in Experiment 1 above, and the slurry was applied with a cotton-tipped swab for one two-minute treatment and then rinsed for one minute in DI water. Teeth were then measured via scintillation counting as in Experiment 1.

Experiment 3—Tubule Occlusion

To determine NovaMin's ability to occlude dentin tubules, the teeth were prepared as described above and then treated using one-minute treatments, for up to six treatments, with a 1:1 slurry of a 7.5 wt% irradiated NovaMin particulate (90 µm–1 µm) and DI water using the same swabbing method described in Experiment 1. After each treatment, the tooth was thoroughly rinsed under a flow of DI water for one minute.

Following treatment with the slurries, a controlled vacuum was applied for one minute via the tube, and each tooth was placed into a certified standard solution of ^{99m}Tc with a 2 µCi/ml concentration. After exposure to the solution, each tooth was then rinsed under a flow of DI water for one minute, and then wiped dry using a dampened lint-free disposable wipe. The uptake of ^{99m}Tc was then measured using a gamma ray detector. The tooth was placed in the detector chamber for five minutes and counts were measured to quantify the radioactive decay. Within this experiment, vacuum-assisted Tc uptake was assumed to relate proportionally to the permeability of the tooth section.

Results

Experiment 1

The results of this experiment can be seen in Figure 1, as expressed in the sum of counts per minute (CPM) resulting from both the ^{45}Ca and ^{32}P isotopes as a function of weight percent (wt%) NovaMin in the dentifrice mixture.

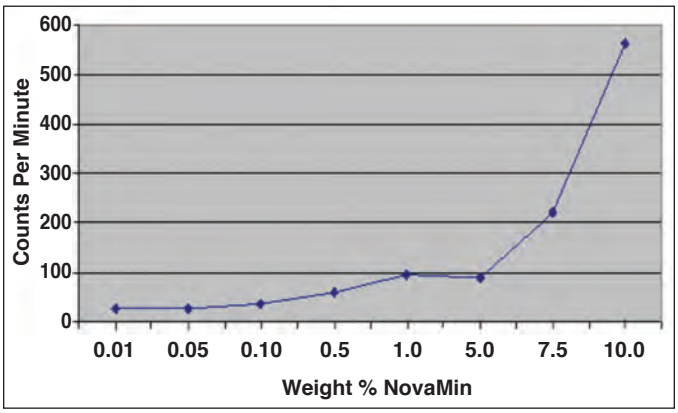


Figure 1. *Ca and P deposition as a function of wt% NovaMin in a dentifrice formulation.*

These results indicate there is a strong dose relationship between the wt% of NovaMin in the dentifrice formulation and new Ca and P deposition. Although there were lower levels of Ca and P deposition measured on the tooth surfaces at concentrations between 0.1 and 0.5 wt%, there was more significant deposition of Ca and P between 1.0 and 5.0 wt%. At above 5.0 wt%, there appears to be an exponential increase in the number of counts from the tooth surface.

To determine if this deposition layer is strongly adhered to the tooth surface, a clean cotton-tipped swab, dampened in DI water, was gently rubbed onto a previously treated tooth surface, and the swab was then subjected to scintillation counting. The resulting counts for both ^{45}Ca and ^{32}P on the swab were not above the background levels, suggesting that no Ca or P from the deposited layer was transferred to the swab.

Experiment 2

The results of this method can be seen in Figure 2, and indicate that finer particle size distribution deposited much higher levels of Ca and P than did the larger range of particle sizes. This is consistent with other experimental work showing the release of Ca and P to be higher in smaller particles of NovaMin due to the higher surface area-to-volume ratios of smaller particles in solution.[16]

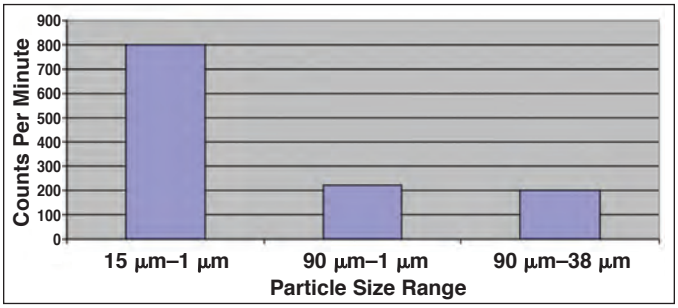


Figure 2. *Ca and P deposition as a function of particle size of NovaMin in a dentifrice formulation.*

Although the use of smaller size NovaMin particles appeared to enhance the reactivity of the NovaMin materials, this enhanced reactivity needs to be taken into consideration in developing a stable dentifrice formulation.

Experiment 3

The results from the ^{99m}Tc study can be seen in Figure 3. The data demonstrate that with repeated exposure of dentin to the isotope, the number of counts of radioactive decay increases. This is indicative of an increased uptake of the radioactive material into the tubules. By contrast, when treated with the dentifrice slurry containing NovaMin, repeated exposure showed only a slight increase in infiltration of the ^{99m}Tc isotope. A statistical analysis, using a paired t-test, shows that there is statistically less uptake of the radioisotope in the NovaMin-treated samples compared with the control ($p < 0.01$) at each time point.

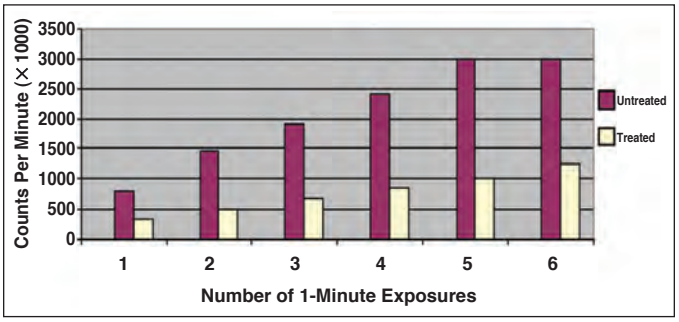


Figure 3. *Reduction of ^{99m}Tc uptake into dentin as a function of NovaMin treatments.*

Surface analysis using scanning electron microscopy (SEM) before and after treatment can be seen in Figure 4, and indicates a significant deposition layer on the dentin surface, with most of the tubules occluded after only one treatment with the dentifrice slurry containing NovaMin. Energy dispersive x-ray spectroscopy (EDS) also confirmed this deposition layer to be rich in Ca and P post-treatment versus the untreated surface.

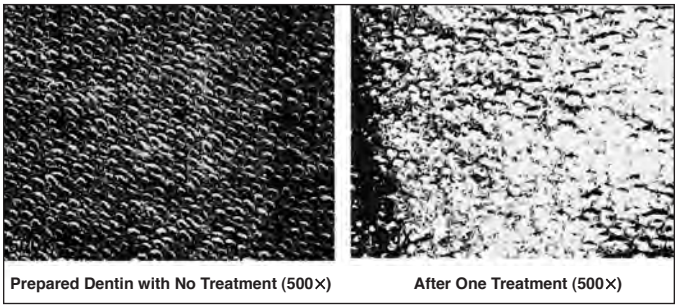


Figure 4. *Prepared dentin before and after NovaMin treatment.*

Discussion

NovaMin is the trade name for an inorganic particulate known as calcium sodium phosphosilicate (abbreviated CSPS). The material is identical in composition to a bioactive glass known as Bioglass® and sometimes referred to as "45S5." This material was originally used as a bone regenerative material in orthopedics, dental, and other hard tissue regenerative areas.[17] There is a wealth of scientific literature that has established and defined a series of reaction steps associated with the CSPS material when subjected to an aqueous environment. It has also been demonstrated that these ionic reactions result in the formation of a hydroxyl carbonate apatite layer (HCA) on the surface of the particles that is almost identical to natural bone mineral.[18] These attributes of the CSPS material led to the development of a specific range of particles that could be used to physically occlude dentin tubules to reduce dentin hypersensitivity.

The successful and long-term efficacy of tubule occluding agents has been subject to much research and debate. There are a number of calcium phosphate- and calcium carbonate-based materials used in combination with organic proteins and amino acids to aid in the deposition of calcium phosphate onto exposed dentin surfaces.[19,20] While all of these materials react while brushing and accomplish their intended task during the one- to two-minute brushing period, the CSPS material is unique in that the particles adhere to the dentin surface and continue to release Ca and P ions once they are deposited onto the tooth surface.[21] Early studies with the CSPS material using SEM and infrared spectroscopy (FTIR) show that not only were there particles adhering on exposed dentin surfaces, but there appeared to be an hydroxycarbonateapatite (HCA) layer on the surface as well.[22]

More recent *in vitro* studies demonstrate that the CSPS material not only occluded the vast majority of tubules with one application, but that these were resistant to acid challenges, and the tenacity of the occlusion was far greater compared with other calcium tubule-occluding technologies.[23] It has been hypothesized that the continued release of ions from the CSPS material deposited on the dentin surface is responsible for this higher level of performance in occluding dentin tubules. Studies have also demonstrated that in human and artificial saliva there is a long-term release of Ca into saliva.[24,25]

The neutron activation studies described here were exploratory in nature, and were performed in order to determine if these techniques have the potential to differentiate between the Ca and P released from the NovaMin particles, and incorporated into dentin and the intrinsic Ca and P of the dentin substrate. By varying the dose and particle size range of NovaMin in these studies, the differences noted suggest that this technique has sufficient merit to be refined further. In Experiment 1, a dose-dependent relationship on the Ca and P counts was clearly demonstrated. Interestingly, there was limited deposition of Ca and P until at least 5% NovaMin was incorporated into the dentifrice formulation. This result strongly suggests a minimum amount of material must be present in order to effectively deposit Ca and P onto the tooth surface, albeit within the exploratory limitations of this study.

In Experiment 2, a significant qualitative effect of particle size on the deposition of Ca and P was observed. Certainly, the surface area of particles and number of particles for a given wt% will increase significantly with decreasing particle size. In the three particle size ranges tested, which are similar to those used in different commercial products, the smallest particle size gave significantly higher levels of Ca and P deposition compared with the other two particle ranges. As the concentration (in wt%) of particles in all three groups was identical, the increased counts must be related to a greater concentration of calcium and phosphate

retained on the tooth surface. Since it is well known that the release of ions from CSPS particles is highly dependent on the exposed surface area, it is likely that the increased counts are due to an increase of reactivity of these finer particles.[26]

In Experiment 3, employing meta-stable Tc, the efficacy of the occlusion of dentin tubules using the CSPS particles was confirmed, and the potential utility of the models was demonstrated. While this experiment was only conducted once (no replicates), the results cannot strictly be quantified, but the count number was numerically different at each treatment point for the NovaMin versus control. Since the same sample was subjected to five repeated treatments (control DI water or CSPS at 7.5 wt%), this study was able to demonstrate that the porosity of the tubules was greatly reduced using the CSPS material, in agreement with previous occlusion-based studies.[27] It is interesting to note that with subsequent treatments, the number of counts of ^{99m}Tc increased dramatically in the control sample, while there were only modest increases in the CSPS-treated samples.

It must be noted that there are limitations to the studies above. First, these were exploratory and not statistically designed to demonstrate quantitative differences. Second, the sample sizes used were small and there could have been variations in material properties due to this small sample size. However, even with these limitations, the techniques clearly showed differences between the particles and control groups, and showed at least qualitative differences in deposition of Ca and P as a function of concentration. These data support the data presented by Burwell, *et al.* using standard *in vitro* techniques.[27]

Conclusions

The data generated from these studies has shown that using a radio-labeled isotope can be useful in supporting the theory of physical tubule occlusion using a calcium sodium phosphosilicate material. It was shown that there is a dose-dependence of NovaMin on the deposition of calcium and phosphate on dental hard tissue and in the *in vitro* efficacy of tubule occlusion. There is an indication that a dose of 5.0 wt% NovaMin or higher in a dentifrice formulation may be required for meaningful calcium phosphate deposition to occur on the tooth surface. The results also demonstrate that the deposition of Ca and P are affected by the particle size and surface area of the CSPS material, and that this deposition is not prevented in the presence of typical dentifrice ingredients. The use of radio isotopes was useful to help demonstrate the uptake of Ca and P into both dentin and enamel tooth structure as a function of CSPS concentration and particle size, as well as demonstrating the tubule occlusive effects of the CSPS material. While adding very useful technical information that helps to explain the mode of action of this material in treating dentin hypersensitivity, the ultimate proof must be through controlled, prospective clinical studies. Future work should be conducted using this technique in more rigorous, statistically designed studies to confirm these results.

Acknowledgment: This study was supported by NovaMin Technology Inc. Publication of this study was supported by GlaxoSmithKline Consumer Healthcare.

For further correspondence with the authors of this paper, please contact Dr. David Greenspan—dspinode@gmail.com.

References

1. Gysi A: An attempt to explain the sensitiveness of dentine. *Br Dent J* 1900; 43:865–868.
2. Addy M. Dentine hypersensitivity**:** New perspectives on an old problem. *Int Dent J* 2002;52(Suppl):367-375.
3. Gillam DG, Seo HS, Bulman JS, Newman HN. Perceptions of dentine hypersensitivity in a general practice population. *J Oral Rehabil* 1999;26:710-714.
4. Brännström M. A hydrodynamic mechanism in the transmission of pain-producing stimuli through dentine. In: *Sensory Mechanisms in Dentine: Proceedings of a Symposium, London, September 24th, 1962*, Anderson DJ, ed. Pergamon, Oxford, pp.73-79, 1963.
5. Orchardson R, Gillam DG. Managing dentin hypersensitivity. *J Am Dent Assoc* 2006;137:990-998.
6. Hodosh M. A superior desensitizer—potassium nitrate. *J Am Dent Assoc* 1974;88:831–832.
7. Markowitz K, Kim S. Hypersensitive teeth. Experimental studies of dentinal desensitizing agents. *Dent Clin North Am* 1990;34: 491-501.
8. Markowitz K, Kim S. The role of selected cations in the desensitization of intradental nerves. *Proc Finn Dent Soc* 1992;88(Suppl 1):39-54.
9. Santiago SL, Pereira JC, Martineli AC. Effect of commercially available and experimental potassium oxalate-based dentin desensitizing agents in dentin permeability: influence of time and filtration system. *Braz Dent J* 2006; 17300-305.
10. Orchardson R, Gillam DG. The efficacy of potassium salts as agents for treating dentin hypersensitivity. *J Orofac Pain* 2000;14:9-19.
11. Pitts NB, Wefel JS. Remineralization/Desensitization: What is known? What is the future? *Adv Dent Res* 2009;21:83-86.
12. Wefel JS. NovaMin: likely clinical success. *Adv Dent Res* 2009;21:40-43.
13. Regina M, Filgueiras T, La Torre G, Hench L. Solution effects on the surface reactions of three bioactive glass compositions. *J Biomed Mater Res* 2004;27:1485–1493.
14. Rehman I , Knowles JC, Bonfield W. Analysis of *in vitro* reaction layers formed on Bioglass using thin-film X-ray diffraction and ATR-FTIR microspectroscopy. *J Biomed Mater Res* Part A 1998;41:162-166.
15. Alfassi ZB. *Chemical Analysis by Nuclear Methods*. John Wiley and Sons, Inc, 1994.
16. Greenspan DC, Zhong ZP, LaTorre GP. Effects of surface area to volume ratio on *in vitro* surface reactions of bioactive glass particulates. In: *Bioceramics*, Anderson OH, Yli-Urpo A, eds., Elsevier Science Ltd, pp.28-33, 1994.
17. Hench LL. Bioceramics: from concept to clinic. *J Am Ceram Soc* 1991;74: 1487-1510.
18. Hench LL, Anderson OH, LaTorre GP. *Proceedings of the 4th International Symposium On Ceramics in Medicine*, Butterworth-Heinemann Ltd., Guildford, 1991.
19. Cross KJ, Huq NL, Reynolds EC. Casein phosphopeptides in oral health—chemistry and clinical applications, *Curr Pharm Des* 2007;13:793-800.
20. Cummins D. Dentin hypersensitivity: from diagnosis to a breakthrough therapy for everyday sensitivity relief. *J Clin Dent* 2009;20(Spec Iss):1-9.
21. Jennings DT, McKenzie KM, Greenspan DC, Clark AE. Quantitative analysis of tubule occlusion using novamin (sodium calcium phosphosilicate). *J Dent Res* 2004;83(Spec Iss A):2416.
22. Litkowski LJ, Hack GD, Sheaffer HB, Greenspan DC. Occlusion of dentin tubules by 45S5 bioglass. In: *Bioceramics - Proceedings of the 10th International Symposium on Ceramics in Medicine.* Sedel L, Rey C, eds. New York, Elsevier Scientific, pp. 411-414, 1997.
23. Burwell AK, Greenspan DC. Dentifrice protection against dentin demineralization in an *in vitro* model. *J Dent Res* 2007;86(Spec Iss A):1764.
24. Burwell AK, Muscle DP. Sustained calcium ion and ph release from calcium phosphate-containing dentifrices. *J Dent Res* 2009;88(Spec Iss A):1936.
25. Grootveld M, Blackburn J, Silwood CJ, Lynch E. Dentifrice induced elevations in salivary calcium levels monitored by ^{1}H NMR. *J Dent Res* 2006;85(Spec Iss C):805.
26. Hench LL, Wilson J. An introduction to bioceramics. In: *Advanced Series in Bioceramics* Vol 1, World Scientific Publishing Company, 1993.
27. Burwell A, Jennings D, Muscle D, Greenspan DC. NovaMin and dentin hypersensitivity—*In vitro* evidence of efficacy. *J Clin Dent* 2010;21(Spec Iss):69-71.

A Clinical Study of the Effect of Calcium Sodium Phosphosilicate on Dentin Hypersensitivity—Proof of Principle

Leonard Litkowski, DDS, MS

Dentsply International
York, PA, USA

David C. Greenspan, PhD

Spinode Consulting
Gainesville, FL, USA

Abstract

- **Objective:** NovaMin® is technically described as amorphous sodium calcium phosphosilicate, and has been shown in laboratory studies to rapidly occlude dentin tubules through the deposition of particles that react to form a protective layer, similar to bone mineral, on the dentin surface. NovaMin was originally developed as a bone regenerative material and is highly biocompatible. The objective of this pilot study was to compare the safety and effectiveness of two prototype formulations containing 2.5% and 7.5% w/w NovaMin to a placebo dentifrice for the treatment of dentin hypersensitivity.
- **Methods:** This was a randomized, double-blind, placebo-controlled pilot study. Sixty-six subjects with a confirmed diagnosis of dentin hypersensitivity were randomized to one of three treatments: 2.5% NovaMin, 7.5% NovaMin, or placebo. Two standard test stimuli, tactile and thermal air, were applied to sensitive cervical dentin surfaces. Subjects recorded the intensity of sensitivity in response to each stimulus on a visual analog scale at baseline, and after two, four, and eight weeks of twice-daily product use. Oral soft tissues were examined and spontaneous reports of adverse experiences were also monitored.
- **Results:** Comparison of the mean change from baseline among the three treatment groups indicated a meaningful reduction in sensitivity scores in the 7.5% group that was significant compared to reductions observed in the placebo control group at all time points.
- **Conclusion:** The results of this study are supportive of the incorporation of NovaMin into products intended for the reduction of dentin hypersensitivity.

(J Clin Dent 2010;21[Spec Iss]:77–81)

Introduction

Thermal, tactile, osmotic, as well as evaporative non-noxious stimuli applied to exposed dentin can elicit a painful response in individuals with hypersensitive teeth. The pain is of short duration and is characterized as being sharp and shooting. Tooth sensitivity is a common complaint and, depending on whether the sensitivity was self-reported or diagnosed, studies of its prevalence have found it to range from 8–40% of adult populations, with a peak incidence between the ages of 20 and 40 years.[1-3] The pain and discomfort associated with dentin hypersensitivity can be bothersome or even extremely troubling to the sufferer. The role of the dental professional is very important for the management of the condition since other factors, including caries, defective restorations, fractured teeth, or occlusal trauma can cause similar symptoms and must be ruled out to confirm the diagnosis of dentin hypersensitivity.[4] In addition, diet and certain oral hygiene practices contribute to erosion or abrasion of tooth structure and lead to exposure of dentin. Therefore, patient education is a necessary component of the treatment and prevention of the condition.[5]

Despite the availability of a variety of in-office and over-the-counter preparations, dentin hypersensitivity remains a chronic condition with acute episodes. While the dentin remains chronically exposed to the oral environment, tubules that are open may become occluded naturally by mineral deposits from saliva or by treatment agents. However, habits and dietary factors, such as acidic foods and beverages, especially when combined with continued abrasion from tooth brushing, may continually degrade, dissolve, or wear away the occluding layer, re-opening tubules, and resulting in an acute episode of sensitivity when the area is further challenged. As a result, the condition has features of both acute and chronic pain that may affect an individual's mood and social behavior, and cause a variable or non-response to treatment.[6]

Given the on-going relationship between the etiologic factors for hypersensitivity, their effect on treatment outcomes, and the quality of life of the sufferer, there is a need for next generation products that are formulated to provide robust and durable tubule occlusion.

In the early 1970s, bioactive glasses were developed as bone regenerative materials because of their similarity to bone mineral. NovaMin® (NovaMin Technology Inc., Alachua, FL, USA) is technically described as inorganic amorphous calcium sodium phosphosilicate (CSPS), and is the branded ingredient found in a number of professional and over-the-counter dental products designed to give immediate and long-lasting relief from tooth sensitivity. The history of the development of this innovation in biomaterials that lead to its application in dentin hypersensitivity is reviewed in detail by Greenspan.[7]

Promising results from early *in vitro* studies gave an indication that NovaMin occluded dentin tubules and could possibly be used to treat dentin hypersensitivity.[8] Therefore, a proof of principle pilot study of an early low-water formulation, containing small particle-size NovaMin, was indicated. The pilot study evaluated

the efficacy, as well as the safety and oral soft tissue tolerance of NovaMin during patient use, and included a placebo. The results of this pilot study have been previously reported in abstract form.[9] Following this pilot study, the dentifrice formulation was further optimized and subsequent clinical studies, conducted in India[10-12] and China,[13] have demonstrated the clinical efficacy and safe use of commercially available dentifrices containing 7.5% and 5% NovaMin for the treatment of dentin hypersensitivity.

Materials and Methods

Study Design

This clinical study was designed to simultaneously enable the detection of the effect of NovaMin on the hypersensitivity response to tactile and thermal air stimuli, as well as make an assessment of any adverse effects in a dose-dependent manner. Prototype formulas (Table I) were developed by direct replacement of a portion of an abrasive silica normally found in a standard "low-water" aqueous dentifrice vehicle to final concentrations of 2.5% and 7.5% w/w NovaMin (Table II). The upper limit of 7.5% was the maximum amount that could be incorporated into the vehicle, while maintaining the optimal physical and chemical properties of the paste. The placebo consisted of the same dentifrice vehicle without NovaMin.

Table I
Dentifrice Composition

Sorbitol 70% Solution
Deionized Water
Sodium Monofluorophosphate
Sodium Saccharin
Glycerin 96% USP
Carboxymethylcellulose
*Sylodent® 750/NovaMin
**Sylodent® 15
Peppermint Flavor
Sodium Lauryl Sulphate
Ethyl Alcohol
FD&C Blue #1

*Abrasive Silica/CSPS- refer to Table II for formula-specific proportion.
**Thickener.

Table II
Abrasive Silica Component

	Placebo	2.5% NovaMin	7.5% NovaMin
Sylodent® 750	10%	7.5%	2.5%
CSPS	0	2.5%	7.5%

The choice of tactile and thermal air stimuli and application method was consistent with guidelines for clinical testing of products for dentin hypersensitivity.[4] This guideline recommends the use of two hydrodynamic stimuli because teeth are often sensitive to multiple stimuli; tactile and cold evaporative air were chosen. Tactile stimuli compress the smear layer and dentin, causing the rapid inward movement of dentinal fluid which in turn activates mechanoreceptors with ensuing painful sensation. Tactile stimuli can be made quantitative by the use of the Yeaple probe, which can be calibrated to deliver a predetermined force to the tooth surface. In addition, a one-second blast of air will also cause fluid movement through evaporation and cooling. Water loss through evaporation induced by an air blast is much higher in the absence of a smear layer.[14] Theoretically, occluding dentin tubules with NovaMin and subsequently a mature HCA layer could reduce water loss and fluid movement in dentin. The intensity of the pain associated with each stimulus was evaluated subjectively by the participant using a visual analog scale (VAS). A VAS is often used in hypersensitivity studies because it is less language-dependent and offers a continuum, rather than a restrictive verbal rating scale. VAS has been found to be reproducible because a high correlation between successive measurements of pain severity has been noted.[15]

Study Population

Prior to recruiting participants, the study was reviewed and approved by the Institutional Review Board at the University of Maryland, and informed consent was obtained from each participant. Inclusion and exclusion criteria were used to identify a population of healthy males and females with dentin hypersensitivity not currently using a desensitizing toothpaste, gel, or other desensitizing products. Study participants were screened for eligibility based on a review of their medical history to exclude those taking concomitant medications that might interfere with the ability to discriminate a pain response, pregnant or lactating females, or anyone with allergies to components of the study products. A full-mouth examination was performed on eligible participants to rule out the presence of any dental pathology that may be causing pain similar to cervical dentin hypersensitivity, and to identify two teeth for inclusion in the study.

Efficacy Assessment

A standardized tactile stimulus using a Yeaple probe, calibrated to deliver a 40-gram force perpendicular to the tooth structure, and a thermal stimulus from a one-second blast of air were applied to all teeth with evidence of cervical dentin exposed by abrasion, erosion, or gingival recession. Immediately following the application of either stimulus, participants rated sensitivity on a 0–100 mm VAS anchored at "None" and "Severe." A rating between 30 and 70 mm on the VAS for each stimulus was necessary for inclusion of that tooth into the study. Values recorded at this visit were considered as baseline measures.

Participants meeting all inclusion criteria with no exclusions were randomly assigned to an eight-week treatment schedule of unsupervised brushing twice a day with one of the three dentifrices; placebo, 2.5% NovaMin, or 7.5% NovaMin. A total of 66 participants, 22 per treatment group, with dentin hypersensitivity were enrolled. Each received a 120 gram tube of dentifrice and a soft toothbrush at baseline and at each follow-up visit.

Tactile and thermal stimuli were again applied to study teeth to measure efficacy after two, four, and eight weeks of product use.

Compliance

Compliance was measured by weighing the toothpaste tubes after collection, calculating paste usage rates, and comparing them across treatment groups at the conclusion of the study.

Safety

An oral soft tissue examination and a calculus evaluation were performed at each clinical visit to assess the safety of the product. Spontaneous reports of adverse events were also collected and tabulated.

Sample Size Determination

The primary outcome was subject response to tactile and thermal stimuli based on VAS scores. A range of six for mean change from baseline score to each weekly end point was assumed. Using 1.5 as a conservative estimate of standard deviation for each group, a sample size of no more than 10 per study group was needed to detect a 40% relative efficacy for a test product over placebo, with a two-tailed alpha of 0.05 and a beta of 0.80. Since this was the first pilot study of NovaMin for this indication, direct comparisons of these assumptions to other studies were not possible. If the mean difference in scores was smaller and/or the standard deviations were larger than assumed, the sample size would increase. Therefore, a sample size of 20 subjects per treatment arm was selected. This sample size was both practical to recruit and consistent with toothpaste studies of other efficacious active ingredients reported in the literature.

Statistical Analysis

The primary outcomes for this pilot study were the thermal and tactile VAS scores at weeks two, four, and eight. The responses among the three treatment groups were compared using a one-way analysis of variance (ANOVA) on the change scores from baseline at two, four, and eight weeks. If the treatment factor was found to be significant at alpha equal to 0.05, then Duncan's Multiple Range test was used to rank group differences. The factors age and sex were also included as covariates in each model.

Results

Baseline Demographics and VAS Scores

A total of 66 participants were randomized to treatment; 22 participants to 2.5% NovaMin, 22 participants to 7.5% NovaMin, and 22 participants to placebo control. All subjects completed the study. Demographics are displayed in Table III. No significant differences in the distribution of males and females, distribution of race, mean age at baseline, mean thermal VAS score at baseline, or mean tactile VAS score at baseline were found among the three treatment groups.

Table III
Baseline Demographics and VAS Scores

	Placebo Control	2.5% NovaMin	7.5% NovaMin
Total Number of Subjects	22	22	22
Male	4	4	4
Female	18	18	18
Mean Age (yrs)	36.7	40.6	39.2
Mean (± SE) Tactile VAS at Baseline	47.5 (2.3)	48.4 (2.2)	49.2 (2.2)
Mean (± SE) Thermal Air VAS at Baseline	48.7 (1.9)	50.0 (1.7)	49.4 (1.8)

Note: There are no significant differences among groups.

Efficacy

Mean tactile VAS scores and mean thermal VAS scores at each follow-up time point are displayed for each treatment group in Figures 1 and 2. Reductions in both air and tactile sensitivity that continue over time are evident for all three groups, with the greatest benefit observable in the 7.5% treatment group. The plots are suggestive of a dose response at weeks two and four that is less evident in the 2.5% group by week eight.

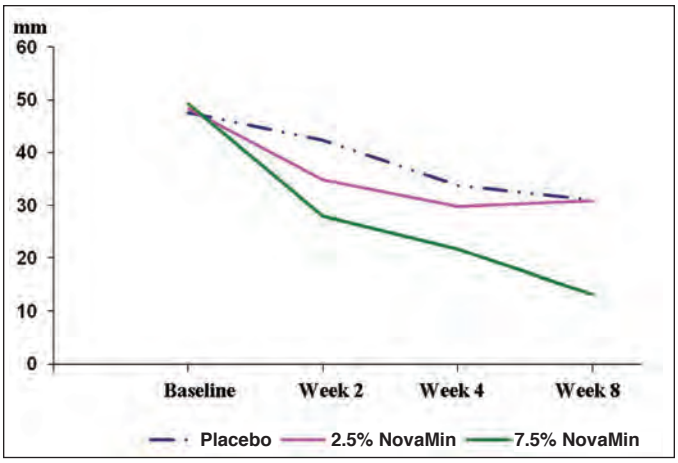


Figure 1. *Mean VAS scores following application of a standard tactile stimulus using a Yeaple probe calibrated to a 40 gram force.*

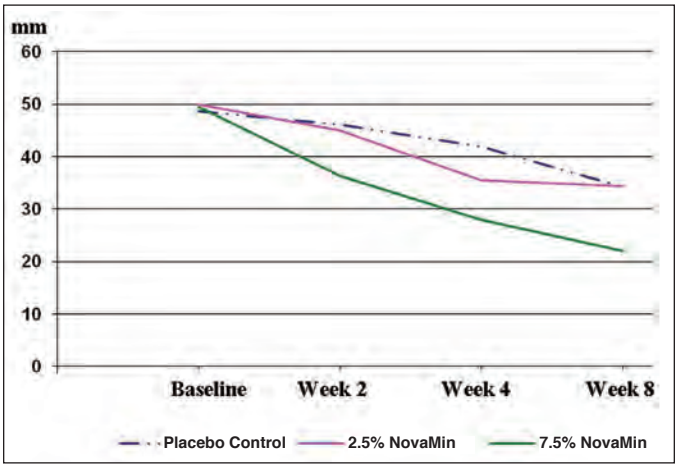


Figure 2. *Mean VAS scores following application of a one-second air blast directed at the exposed dentin surface.*

Statistical comparisons of the mean change from baseline among the three treatment groups (Table IV and V) indicate a significant difference between the 7.5% group and placebo control at all time points, no significant difference between the 2.5% group and placebo control at any time point, and a significant difference between the 2.5% and 7.5% groups at week eight for the air and tactile parameters.

Compliance

The control group used an average of 142.4 grams of dentifrice over the eight-week study. The 2.5% and 7.5% groups used an average of 161.2 and 144.5 grams, respectively. The amount of dentifrice used between clinical visits was also calculated and compared. There were no statistically significant differences

Table IV
Mean ± SE Change from Baseline
(% Reduction from Baseline)
Tactile VAS (mm)

	Placebo Control	2.5% NovaMin	7.5% NovaMin	Treatment Difference p-value
Week 2	5.1 ± 3.4 (11%)	13.6 ± 4.3 (28%)	21.1 ± 3.7* (43%)	0.016
Week 4	13.7 ± 3.6 (29%)	18.6 ± 4.2 (38%)	27.5 ± 3.6* (55%)	0.049
Week 8	16.5 ± 3.3 (35%)	17.6 ± 5.4 (36%)	36.0 ± 3.1*§ (73%)	0.001

*indicates significant difference vs. placebo control.
§indicates significant difference vs. 2.5% NovaMin.
Note: All values are indicative of a reduction in response compared to baseline. Statistical analysis based on comparison of mean change from baseline. Significance = $p < 0.05$.

Table V
Mean ± SE Change from Baseline
(% Reduction from Baseline)
Thermal Air VAS (mm)

	Placebo Control	2.5% NovaMin	7.5% NovaMin	Treatment Difference p-value
Week 2	2.6 ± 2.1 (5%)	5.1 ± 3.9 (9%)	13.1 ± 2.9* (26%)	0.016
Week 4	6.8 ± 3.1 (14%)	14.5 ± 4.4 (28%)	21.5 ± 3.1* (43%)	0.049
Week 8	14.5 ± 3.6 (28%)	15.5 ± 4.7 (30%)	27.4 ± 3.3*§ (55%)	0.001

*indicates significant difference vs. placebo control.
§indicates significant difference vs. 2.5% NovaMin.
Note: All values are indicative of a reduction in response compared to baseline. Statistical analysis based on comparison of mean change from baseline. Significance = $p < 0.05$.

among the treatment groups in the amount of dentifrice used at any time point.

Safety

Examiner Findings. All participants had a soft tissue and calculus evaluation at baseline. Over the eight-week treatment period, soft tissue abnormalities not present at baseline were reported for two participants in the control group, two in the 2.5% group, and five participants in the 7.5% group. All were mild in nature and the majority were related to inflammation of the gingival area. All but one resolved by the conclusion of the study, therefore it was followed to resolution.

The examiner also scored each participant as having a minimum, moderate, or severe amount of overall calculus. At baseline, 91% of study participants had a minimum amount of calculus, and using this measure the proportion of participants remained stable over the course of the study.

Spontaneous Reports by Subjects. Of the 66 participants, approximately 57% reported at least one adverse experience during the study. The majority were not orally related; for example, sinus condition, cold, or allergy. The profile of event rates in the three treatment groups was similar.

Of the 66 participants, three participants in the control group and four participants in the 7.5% group spontaneously reported at least one adverse event that was assessed as being "Possible," "Probable," or "Not Known" in the relationship to study treatment. All events related to inflammation of oral soft tissues, and it is likely that there is some overlap with the examiner findings from the oral soft tissue examinations.

Discussion

This proof of principle pilot study clearly demonstrated that NovaMin technology, delivered in a dentifrice vehicle, reduces the intensity of pain associated with the application of standardized stimuli to exposed sensitive dentin. As is common with most sensitivity trials, all three formulations reduced the response to standardized tactile and thermal stimuli. The greatest benefit was observed at the highest concentration of NovaMin tested (Figures 1 and 2). Compared to the placebo formula, the reduction in clinical response to both stimuli associated with the use of 7.5% NovaMin was statistically significant at the two-week time point. The effects of treatment were cumulative since the reduction in pain continued to increase, reaching a maximum after eight weeks of brushing, while maintaining a statistically significant difference compared to placebo at every time point tested (Tables IV and V). The reduction in pain intensity associated with a tactile challenge was more pronounced than the reduction associated with the thermal air challenge. This supports the hypothesis that exposed dentin may be more resistant to compressive forces due to tubule occlusion with NovaMin particles and subsequent mineralization to form HCA within the tubule and on the dentin surface.

A particular strength of this pilot study was that it was placebo-controlled. All three dentifrices tested in this pilot study were based on a standard aqueous dentifrice composition (Table I), but the components of the abrasive system differed (Table II). The placebo response observed in the pilot study is consistent with other dentin hypersensitivity studies in which placebo responses in the range of 20–60% reduction compared to baseline have been reported.[6] Such responses are not unique to dentin hypersensitivity studies, but are observed widely across therapeutic categories and are related to a number of factors. While it is not the intention of this pilot study to report on the multiple factors contributing to the placebo effect in great depth, it is worth noting that in addition to the psychological aspects of the placebo effect, the placebo formulas used in hypersensitivity studies have "active" components. It is well documented that silica can effectively occlude dentin tubules and that the deposit is resistant to mild abrasion or an erosive challenge.[16,17] Fluoride has also been thought to marginally contribute to the desensitizing effect, and these dentifrices contained sodium monofluorophosphate at anticaries levels.[18] In addition, placebo effects arise from subconscious associations between recovery and the experience of being treated. Given that design controls were used, especially blinding to treatment assignment, presumably these associations were being made by all participants in all three treatment groups. Therefore, the significant difference in effect between the

7.5% concentration of NovaMin and the placebo would suggest that the mode of action of silica with NovaMin technology was better than silica alone. A series of *in vitro* studies that help explain this advantage has recently been reviewed.[19] These studies demonstrate that when applied as a slurry, NovaMin will immediately become attracted to an exposed dentin surface and occlude more dentin tubules than a comparative professional product based on amorphous calcium phosphate (ACP).

This pilot study was designed to demonstrate a dose response. The performance of the lower 2.5% concentration would suggest that the availability of NovaMin from the formulation was not high enough at this concentration to maintain the therapeutic range needed to be consistently effective in this study population. Recent *in vitro* studies confirm that NovaMin concentrations of 5% or higher are required.[20] Mild gingival inflammation was observed in all treatment groups. The number of subjects in each treatment group was small (n = 22), making it necessary to interpret the safety data conservatively, but with some caution. The distribution of individual findings suggests a slightly higher incidence of gingival inflammation in the 7.5% group. Retrospectively, the inflammation could have been associated with the frequent use of the new toothbrush which was dispensed at every treatment visit. It is also possible, given the reactive nature of NovaMin, that the material began to release calcium and phosphate into the aqueous environment of the dentifrice, resulting in an elevated pH. The mild intensity did not cause anyone to discontinue participation in the study, however. Subsequent to this pilot study, the manufacturer has reformulated the product in an anhydrous vehicle, and commercial dentifrice formulations containing 7.5% and 5% NovaMin in the anhydrous vehicle have been tested in several clinical studies in India and China. These studies span a range of designs that compare dentifrices containing NovaMin to non-desensitizing dentifrices and other commercially available products containing well-established desensitizing ingredients, such as potassium nitrate, strontium chloride, and stannous fluoride. The results of these studies demonstrate the clinical benefit of the use of dentifrices containing NovaMin for the treatment of dentin hypersensitivity.

Conclusion

The results of this pilot study support the conclusion that NovaMin, delivered by brushing twice daily with a dentifrice, has a beneficial effect by reducing the intensity of the sensitivity response to tactile and thermal stimuli applied to exposed sensitive cervical dentin surfaces.

Acknowledgments: The authors would like to thank Ms. Katie Quinlan for her expert management of the study at the University of Maryland. The authors also thank Linda Gendreau, DDS, MS (Gainesville, FL) for assistance with editing this manuscript; her contribution was funded by GlaxoSmithKline Consumer Healthcare, Weybridge, Surrey, UK. This study was supported by USBiomaterials, Jacksonville Beach, FL, USA. Publication of this study was funded by GlaxoSmithKline Consumer Healthcare.

For further correspondence with the author(s) of this paper, contact Dr. David Greenspan—dspinode@gmail.com.

References

1. Addy M. Dentine hypersensitivity: definition, prevalence, distribution and aetiology. In: *Tooth Wear and Sensitivity*, Addy M, Embery G, Edgar WM, Orchardson R, eds. Martin Dunitz Ltd, London, pp. 239-245, 2000.
2. Graf HE, Galasse R. Morbidity, prevalence and intra-oral distribution of hypersensitive teeth. *J Dent Res* 1997;56(Spec Iss):479.
3. Flynn J, Galloway R, Orchardson R. The incidence of 'hypersensitive' teeth in the West of Scotland. *J Dent* 1985;13:230-236.
4. Holland GR, Narhi MN, Addy M, Gangarosa L, Orchardson R. Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *J Clin Periodontol* 1997;24:808-813.
5. Canadian Advisory Board on Dentin Hypersensitivity. Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. *J Can Dent Assoc* 2003;69:221-226.
6. Curro FA, Friedman M, Leight R. Design and conduct of clinical trials on dentine hypersensitivity. In: *Tooth Wear and Sensitivity*, Addy M, Embery G, Edgar WM, Orchardson R, eds. Martin Dunitz Ltd, London, pp. 299-314, 2000.
7. Greenspan DC. NovaMin® and tooth sensitivity—an overview. *J Clin Dent* 2010;21(Spec Iss):61-65.
8. Litkowski L, Hack GD, Sheaffer HB, Greenspan DC. Occlusion of dentin tubules by 45S5 Bioglass®. *Bioceramics* 1997;10:411-414.
9. Litkowski L. Pilot clinical and *in vitro* studies evaluating NovaMin® in desensitizing dentifrices. *J Dent Res* 1998;77(Spec Iss):747.
10. Pradeep AR, Sharma A. Comparison of clinical efficacy of a dentifrice containing calcium sodium phosphosilicate to a dentifrice containing potassium nitrate and to a placebo on dentinal hypersensitivity: A randomized clinical trial. *J Periodontol* 2010;81:1167-1173.
11. Sharma N, Roy S, Kakar A, Greenspan DC, Scott R. A clinical study comparing oral formulations containing 7.5% calcium sodium phosphosilicate (NovaMin), 5% potassium nitrate, and 0.4% stannous fluoride for the management of dentin hypersensitivity. *J Clin Dent* 2010;21(Spec Iss):88-92.
12. Salian S, Thakur S, Kulkarni S, LaTorre G. A randomized controlled clinical study evaluating the efficacy of two desensitizing dentifrices. *J Clin Dent* 2010;21(Spec Iss):82-87.
13. Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J, Tai BJ. Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (novamin) for the treatment of dentin hypersensitivity. *Am J Dent* 2008; 21:210-214.
14. Pashley DH. Mechanisms of dentin sensitivity. *Dent Clin North Am* 1990; 34:449-473.
15. Clark GE, Troullos ES. Designing hypersensitivity clinical studies. *Dent Clin North Am* 1990;34:531-544.
16. Jackson RJ, Duke SA, Wicks MA, McDonald FE. The effects of antisensitivity dentifrices on subjects consuming acid diets. *J Dent Res* 1990;69(Spec Iss):268.
17. Absi EG, Addy M, Adams D. Dentine hypersensitivity: uptake of toothpastes onto dentine and effects of brushing, washing and dietary acid—SEM *in vitro* study. *J Oral Rehabil* 1995;22:175-182.
18. Pearce NX, Addy M, Newcombe RG. Dentin hypersensitivity: a clinical trial to compare 2 strontium desensitizing toothpastes with conventional fluoride toothpaste. *J Periodontol* 1994;65:113-119.
19. Burwell A, Jennings D, Muscle D, Greenspan DC. NovaMin and dentin hypersensitivity—*In vitro* evidence of efficacy. *J Clin Dent* 2010;21(Spec Iss):66-71.
20. LaTorre G, Greenspan DC. The role of ionic release from NovaMin (calcium sodium phosphosilicate) in tubule occlusion: An exploratory *in vitro* study using radio-labeled isotopes. *J Clin Dent* 2010;21(Spec Iss):72-76.

A Randomized Controlled Clinical Study Evaluating the Efficacy of Two Desensitizing Dentifrices

Dr. Sowmya Salian Dr. Srinath Thakur Dr. Sudhindra Kulkarni

Department of Periodontics and Implantology
SDM College of Dental Sciences and Hospital
Dharwad, India

Guy LaTorre

NovaMin Technology Inc.
Alachua, FL, USA

Abstract

- **Objective:** The primary aim of this study was to compare the *in vivo* efficacy and safety of dentifrices containing either 5% NovaMin® or 5% potassium nitrate, and a non-desensitizing dentifrice, on dentin hypersensitivity in a four-week, double-blind clinical study among a population in south India. In addition, a companion scanning electron microscopy evaluation was performed to demonstrate whether or not the test products occlude open dentin tubules *in vitro*.
- **Methods:** Thirty volunteers with tooth sensitivity were recruited, and a double-blind, randomized, parallel, controlled clinical trial was conducted in a hospital setting. Clinical evaluation for dentin hypersensitivity was done using tactile, air blast, and cold water methods. Following baseline measures, subjects were randomly divided into three groups and treated as follows: Group A—dentifrice containing 5% potassium nitrate; Group B—dentifrice containing 5% NovaMin; and Group C—dentifrice containing no desensitizing ingredients. Clinical evaluations were repeated after two and four weeks of product use.
- **Results:** Compared to baseline, there was a significant decrease in dentin hypersensitivity in Groups A and B following four weeks' use of the dentifrice containing 5% potassium nitrate and the dentifrice containing 5% calcium sodium phosphosilicate (NovaMin), respectively. There was a statistically greater reduction in hypersensitivity at both two and four weeks following use of the dentifrice containing NovaMin compared with the use of a non-desensitizing dentifrice, as well as the dentifrice containing potassium nitrate. Air and cold water scores were significantly lower following four weeks' use of the potassium nitrate dentifrice compared to the non-desensitizing dentifrice. Tubule occlusion was observed in the companion *in vitro* study following treatment with 5% NovaMin, but not after treatment with the 5% potassium nitrate or non-desensitizing dentifrices.
- **Conclusion:** The results suggest that the dentifrice containing 5% NovaMin occludes dentin tubules, and provides rapid and significantly more relief from dentin hypersensitivity in four weeks compared to a dentifrice containing 5% potassium nitrate or a non-desensitizing dentifrice. All three dentifrices tested in this study were well-tolerated.

(J Clin Dent 2010;21[Spec Iss]:82–87)

Introduction

Dentin hypersensitivity is characterized by pain of short duration arising from exposed dentin in response to stimuli, typically thermal, evaporative, tactile, osmotic, or chemical, and which cannot be attributed to any other dental defect or pathology.[1] The response varies substantially from person to person due to differences in tolerance, environmental factors, and emotional status.

Hypotheses have been put forth regarding the desensitizing effect of various compounds on dentin hypersensitivity. To date, research has concentrated on the hydrodynamic theory of dentin hypersensitivity,[2-4] which proposes that stimulus transmission is due to the rapid shift of fluid movement in either direction within the dentin tubules, stimulating mechanoreceptors in or near the pulp. Increased sensitivity may, therefore, be due to an increase in fluid flow within the tubules resulting from the absence of the smear layer and probable removal of some tubule-occluding material.[5] The corollary to this is that blocking the tubules and/or reintroducing the smear layer may reduce stimulus transmission across dentin, and consequently reduce sensitivity.

NovaMin® is amorphous sodium calcium phosphosilicate that has been developed as a fine particulate to physically occlude dentin tubules. It has previously been reported to be effective at concentrations of 7.5% in an anhydrous dentifrice formulation in one study elsewhere in India,[6] and at a concentration of 5% in Chinese[7] and Indian[8] populations. The aim of this study was to evaluate the safety and effectiveness of 5.0% NovaMin in an anhydrous dentifrice formulation in an Indian population. Three dentifrices containing either 5% potassium nitrate (positive control) or 5.0% NovaMin (experimental dentifrice) and a dentifrice containing neither potassium nitrate nor NovaMin (negative control) were evaluated as a treatment for dentin hypersensitivity in a dental hospital setting in south India. The study was a single-center, randomized, double-blind, parallel-group design with a duration of four weeks. The study included 30 subjects, and the protocols for the study were followed as per the guidelines for the design and conduct of clinical trials on dentin hypersensitivity.[1]

Materials and Methods

Clinical Study Design

This was a single-center, randomized, controlled, double-blind study. The study commenced following approval by the Ethics Committee of SDM College of Dental Sciences and

Hospital, Dharwad, India. Patients with a history of tooth hypersensitivity, who were seeking treatment in the outpatient dental department of SDM Dental College in the years 2008–2009, were recruited for a four-week study based on their subjective complaint of dental hypersensitivity. The study was explained to prospective subjects, and informed consent was obtained for their willingness to participate.

Inclusion Criteria. The inclusion criteria required patients be between the ages of 20 and 50 years, in good general health, having at least 20 natural permanent teeth, and a history of hypersensitivity to hot, cold, or sour stimuli on at least two teeth. All patients were evaluated to ensure that they were currently using a toothbrush and toothpaste for their oral hygiene procedures, and had consented to be included in the trial.

Exclusion Criteria. Patients with active cervical caries or deep abrasion requiring a Class V filling, chipped teeth, or fractured cusps were excluded from the study. In addition, a tender tooth in the same quadrant as the hypersensitive teeth, and patients using any type of desensitizing therapy for the last six months were excluded. Subjects with a history of chronic use of anti-inflammatory and analgesic medication, pregnant or lactating females, those with a history of chronic regurgitation of acids, and those who have undergone periodontal surgery in the preceding six months were also excluded.

After completing a subjective evaluation for dentin hypersensitivity, patients were enrolled into the study. Hypersensitivity was verified clinically by application of light strokes of a dental explorer along the cervical margins/areas of all the teeth present. All the subjects underwent oral prophylaxis and observed a two-week wash-out period, during which time they followed their normal hygiene practices. At baseline and at the two- and four-week follow-up, the patients were assessed for subjective change in hypersensitivity by inquiring whether they perceived a reduction in the severity of hypersensitivity after the treatment was initiated. The subjective data were not analyzed statistically. Visual analogue scale (VAS) scores, indicating the intensity of dentin hypersensitivity following application of tactile and thermal stimuli, were then recorded.

Clinical Evaluation of Hypersensitivity

The objective assessment of dentin hypersensitivity was done using the following three methods in order:

Tactile Method. This method was carried out first. The teeth reported to be hypersensitive by the patients were examined with a dental explorer, and slight pressure was applied. Then the patient response to the stimuli was recorded on a standardized ten centimeter (cm) VAS, where one end of it denotes no pain (0) and the other end denotes the worse pain the patient has ever experienced (10 cm). The patients were asked to tick on the VAS depending on the intensity of pain they experienced. The test was performed three times and the average final score was recorded. The time gap between each test was approximately ten minutes.

Air Method. A standard air/water syringe with restricted air stream (60 psi) was directed towards the sensitive portion of the tooth, perpendicular to the long axis of the tooth, for the duration of one second at a distance of about 0.5 cm. Adjacent teeth were protected by the operator's fingers and cotton rolls. The patient's response was recorded on a 10 cm VAS. The test was repeated three times and the average final score was recorded. The time gap between each test was approximately ten minutes. Those teeth with a VAS score between four and ten were selected (10 = severe pain, 0 = no pain).

Cold Water Method. This method was performed approximately ten minutes after the air blast test. The tooth reported to be sensitive by the patient was isolated with cotton rolls. Cold water was delivered in the form of freshly melted ice, applied immediately to the buccal cervical region using a micropipette. Patient's response on a 10 cm VAS was measured. The test was repeated three times and the average final score was recorded. The time between each test was approximately ten minutes. Those teeth between the VAS score of four and ten cm were selected (10 = severe pain, 0 = no pain).

Products Tested

Three commercially available dentifrices were used for the study.

Group A (positive control): 5% potassium nitrate dentifrice (Sensodent—K, Indoco Remedies Ltd. Mumbai, India);

Group B (test dentifrice): 5% NovaMin dentifrice (SHY-NM, Group Pharmaceuticals Limited, Mumbai, India).

Group C (negative control): Sodium monofluorophosphate (1,000 ppm fluoride) Colgate® Dental Cream (Colgate-Palmolive, India).

The dentifrices were supplied in their marketed packages, but were overwrapped to conceal their identity. After the collection of the baseline data, the subjects were randomly divided into three groups of ten subjects each. Each group was designated A, B, or C, and provided with one of the dentifrices. In order to maintain the double-blind nature of the study, the dentifrices were dispensed by a third party so that neither the examiner nor the patients knew the contents of the toothpaste.

Each patient was also provided with an adult soft-bristle toothbrush and was advised to put one-half inch of the assigned dentifrice on the brush. The patients were instructed to brush their teeth in their usual manner for two minutes, twice daily. Patients were instructed not to eat or drink anything within a half hour of brushing with the dentifrices. Patients were recalled at two and four weeks for the measurement of tooth sensitivity by the three methods. At the recall visits, all the used dentifrice tubes were returned and new material was dispensed. During the study period, patients were not permitted to use other oral hygiene products, use any other dental treatment for hypersensitive teeth, or use drugs such as analgesics that may alter the pain perception within 24 hours of the assessment days.

Safety

At each recall visit, the examiner evaluated the oral soft tissues for any signs of adverse reactions. Spontaneous reports of any adverse reactions were also monitored.

Statistical Methods

Statistical analysis of the clinical results was performed using an ANOVA to determine any significant baseline differences in the stratification of the groups. Paired t-tests were performed to determine within-group differences at each time point. An ANCOVA of the group effects at each time point was performed.

Where indicated, a Tukey *post hoc* pair-wise comparison was carried out to determine differences between groups at each time point using $p < 0.05$ as a significance level. All analyses were performed using Sigma Stat and Sigma Plot 9.0.

Companion In Vitro *Study Design*

Twelve dentin discs were obtained by sectioning six freshly extracted caries-free molars. The discs were split into halves and divided into three groups corresponding to one of the test dentifrices. Discs in each group were brushed intermittently by a manual method using an adult soft-bristle toothbrush with one of the test dentifrices. The total accumulated times of brushing were two, ten, 30, and 120 minutes. Prior to application of the test dentifrices, the disc was ultrasonicated in distilled water and then etched with citric acid to remove the smear layer. Following treatment, the discs were prepared for SEM imaging by sputter-coating with palladium.

Results

Clinical Efficacy

Baseline Demographics and VAS Scores. A total of 30 subjects were enrolled into the study. Demographics and baseline VAS scores are displayed in Tables I and II, respectively. An ANOVA of baseline sensitivity scores indicated no significant main effects for the groups ($p = 0.36$, $p = 0.96$, and $p = 0.49$ for tactile, air, and ice, respectively). Since the baseline scores for all three groups were similar and did not show any significant differences, these scores were used as covariates for the ANCOVA.

Significant Improvement Compared to Baseline. Paired t-tests for each group were carried out comparing sensitivity for tactile, air, and cold water at time points two and four weeks to baseline. Two-week sensitivity scores for all three methods were also compared to four-week scores. The results, displayed in Tables III, IV, and V, show that use of the positive control and the test product resulted in reduced tactile, air, and cold water sensitivity compared to baseline, and that the clear trend was for increasing reductions in dentin hypersensitivity over time. When an intragroup comparison was conducted, Group A (5% potassium nitrate dentifrice) did show a statistically significant difference between baseline and 4 weeks, and between two weeks and four weeks for both the air and cold water test. However, it did not show significant differences between baseline and two

Table I
Demographic Data

	Group A 5% Potassium Nitrate	Group B 5% NovaMin	Group C Negative Control
Number of Subjects	10	10	10
Male	6	6	5
Female	4	4	5
Mean Age (years)	38	39.4	38.2

Table II
Baseline VAS* Scores (cm)

	Tactile		Air		Cold Water	
Groups	Mean	SD	Mean	SD	Mean	SD
A	3.56	0.71	5.69	0.58	6.92	0.80
B	3.99	0.84	5.72	1.06	6.87	1.19
C	3.53	0.85	5.61	1.28	6.33	1.59
F-value	1.04		0.03		0.72	
p-value	0.37		0.97		0.49	

Statistical analysis performed using ANOVA.
*VAS is a standardized 10 cm scale in which one end denotes "No Pain" (0) and the other end denotes "Worst Pain Ever" felt by the patient.
A = 5% potassium nitrate dentifrice, B = 5% NovaMin dentifrice, C = negative control dentifrice.

Table III
Comparison of Baseline, Two Weeks, and Four Weeks (Group A, 5% Potassium Nitrate)

		Mean	SD	p-value
Tactile	Baseline	3.56	0.70	
	2 Weeks	3.51	0.62	0.26
	Baseline	3.57	0.70	
	4 Weeks	2.90	0.89	0.03
	2 Weeks	3.51	0.62	
	4 Weeks	2.90	0.89	0.03
Air	Baseline	5.70	0.58	
	2 Weeks	5.65	0.60	0.49
	Baseline	5.70	0.58	
	4 Weeks	4.60	0.41	0.00
	2 Weeks	5.65	0.60	
	4 Weeks	4.60	0.41	0.00
Cold Water	Baseline	6.92	0.80	
	2 Weeks	6.67	0.67	0.01
	Baseline	6.92	0.80	
	4 Weeks	5.43	0.49	0.00
	2 Weeks	6.67	0.67	
	4 Weeks	5.43	0.50	0.00

Statistical analysis performed using paired t-tests.

Table IV
Comparison of Baseline, Two Weeks, and Four Weeks (Group B, 5% NovaMin)

		Mean	SD	p-value
Tactile	Baseline	3.96	0.80	
	2 Week	2.55	0.80	0.00
	Baseline	3.96	0.80	
	4 Week	0.96	0.8I	0.00
	2 Week	2.55	0.81	
	4 Week	0.96	0.81	0.00
Air	Baseline	5.77	1.02	
	2 Week	3.81	1.10	0.00
	Baseline	5.77	1.02	
	4 Week	1.99	1.22	0.00
	2 Week	3.81	1.10	
	4 Week	1.99	1.22	0.00
Ice	Baseline	6.85	1.14	
	2 Week	4.45	1.39	0.00
	Baseline	6.85	1.14	
	4 Week	2.37	1.20	0.00
	2 Week	4.45	1.39	
	4 Week	2.37	1.20	0.00

Statistical analysis performed using paired t-tests.

Table V
Comparison of Baseline, Two Weeks, and Four Weeks (Group C, Negative Control)

		Mean	SD	p-value
Tactile	Baseline	3.55	0.81	
	2 Week	3.55	0.81	—
	Baseline	3.55	0.81	
	4 Week	3.35	0.79	0.08
	2 Week	3.55	0.81	
	4 Week	3.35	0.79	0.08
Air	Baseline	5.67	1.23	
	2 Week	5.70	1.25	0.34
	Baseline	5.67	1.24	
	4 Week	5.41	1.29	0.11
	2 Week	5.70	1.25	
	4 Week	5.41	1.29	0.07
Ice	Baseline	6.36	1.51	
	2 Week	6.36	1.51	—
	Baseline	6.36	1.51	
	4 Week	5.97	1.52	0.05
	2 Week	6.36	1.51	
	4 Week	5.97	1.52	0.05

Statistical analysis performed using paired t-tests.

weeks in all the three methods. Group B (5% NovaMin) did show a statistically significant difference between baseline and two weeks, and also four weeks, in all the three methods. With the exception of cold water at the baseline/week four and the two-week/four-week intervals, there was no statistically significant difference seen at any time interval in any of the three methods in Group C (negative control).

Subjective Evaluation. At every recall, the patients did find a subjective reduction in hypersensitivity.

Significant Difference Among Treatments

Using an ANCOVA, with data from two weeks and four weeks as dependent variables and baseline values as covariates, the overall tactile, air, and cold water sensitivity scores demonstrated a significant difference among groups and a significant difference over the four-week study period (Table VI). *Post hoc* pair-wise comparisons were carried out using Tukey's analysis. The results are displayed in Table VII.

Postive Control Compared to Negative Control. After four weeks of use, air and cold water scores in the postive control group (5% potassium nitrate dentifrice) were significantly

Table VI
Comparison of Three Groups at Two Weeks and Four Weeks by ANCOVA with Baseline as Covariate

	Tactile		Air		Ice	
	2 Weeks Mean	4 Weeks Mean	2 Weeks Mean	4 Weeks Mean	2 Weeks Mean	4 Weeks Mean
Group A	3.51	2.89	5.64	4.59	6.67	5.42
Group B	2.44	0.79	3.57	1.72	4.23	2.11
Group C	3.53	3.41	5.64	5.48	6.33	6.07
F-value	71.71	57.19	127.58	154.33	165.81	198.80
p-value	0.00	0.00	0.00	0.00	0.00	0.00

A = 5% potassium nitrate dentifrice, B = 5% NovaMin dentifrice, C = negative control dentifrice.

Table VII
Significant Differences Among Treatments

	Tactile		Air		Ice	
	2 Weeks	4 Weeks	2 Weeks	4 Weeks	2 Weeks	4 Weeks
B-A*	0.00	0.00	0.00	0.00	0.00	0.00
A-C§	0.99	0.16	0.99	0.00	0.09	0.02
B-C*	0.00	0.00	0.00	0.00	0.00	0.00

Statistical analysis performed using Tukey *post hoc* pair-wise comparison.
A = 5% potassium nitrate dentifrice, B = 5% NovaMin dentifrice, C = negative control dentifrice.
Note: *significant differences are in favor of Group A, §significant differences are in favor of Group A.

($p < 0.05$) lower than in the negative control group (Colgate Dental Cream). Compared to the negative control, a trend toward significantly lower tactile scores was noted after four weeks' use of the positive control. A trend toward lower cold water scores was also noted after two weeks' use of the positive control compared to the negative control.

5% NovaMin Compared to Negative and Positive Controls. At all time points tested, tactile, air, and cold water scores for the the 5% NovaMin group (Group B, test product) were significantly ($p < 0.05$) lower than scores for both the 5% postassium nitrate group (Group A, positive control) and the Colgate Dental Cream group (Group C, negative control).

Safety

No side effects were reported.

In Vitro *Results*

Qualitative examination of the dentin tubules observed by scanning electron micrography revealed tubule occluding properties for the 5% NovaMin dentifrice as early as ten minutes, and partial to complete occlusion observed after 120 minutes of brushing with the toothpaste. Discs treated with 5% potassium nitrate dentifrice or the negative control dentifrice showed no such properties at any time point. Representative SEMs illustrating these differences are found in Figures 1 a, b, c, and d.

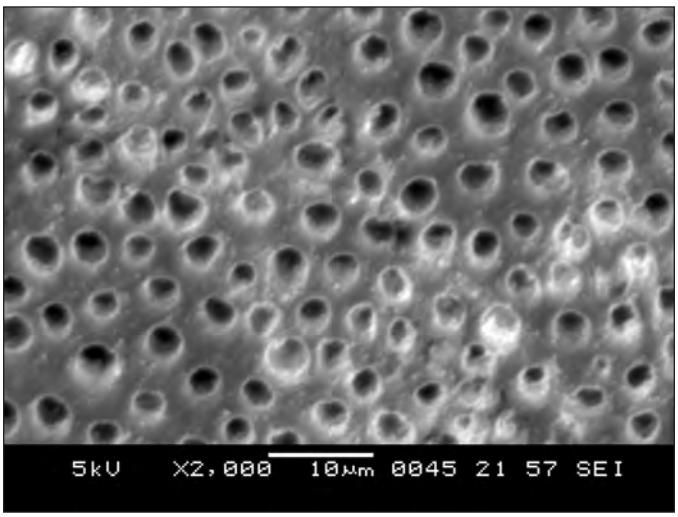


Figure 1a. *SEM image of dentin disc treated with 5% NovaMin dentifrice after 10 minutes.*

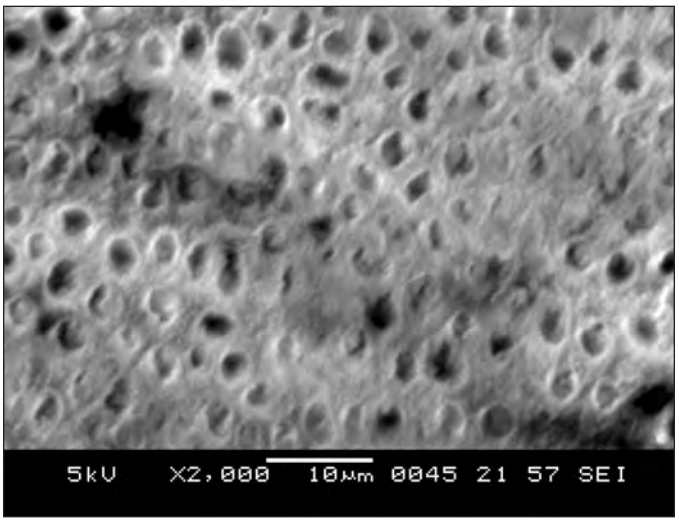


Figure 1b. *SEM image of dentin disc treated with 5% NovaMin dentifrice after 120 minutes.*

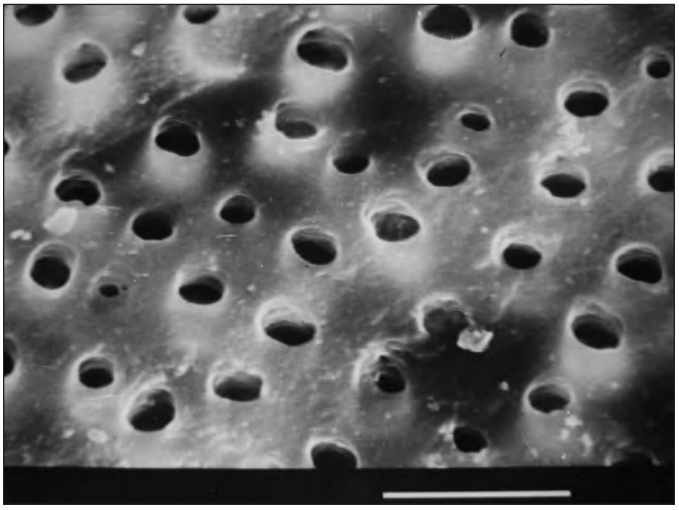


Figure 1c. *SEM image of dentin disc treated with 5% potassium nitrate dentifrice.*

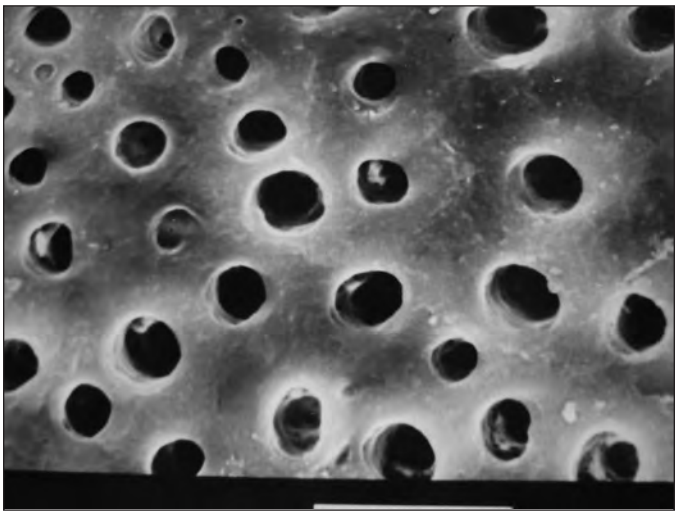


Figure 1d. *SEM image of dentin disc treated with control dentifrice.*

Discussion

The objective of this study was to evaluate the efficacy and safety of a new desensitizing dentifrice formulation containing 5% NovaMin in an Indian population. A commercially available dentifrice containing 5% potassium nitrate was used as a positive control, and a fluoride dentifrice without desensitizing ingredients, also commercially available, was used as the negative control. Neither the test dentifrice nor the positive control contained fluoride.

The results of this clinical trial demonstrate that the demographics of the test population in south India are well within the range of age and gender reported to be affected by dentin hypersensitivity.[9] Within-group and comparative analyses of results for the dentifrice containing 5% potassium nitrate used as the positive control in this study conform to a number of clinical studies that have been recently reviewed, and showed 5% potassium nitrate to be effective after two to four weeks' use.[10] The use of the negative control dentifrice did not reduce sensitivity scores to a significant extent. However, as is frequently observed in clinical studies of dentin hypersensitivity, a modest, positive response to the negative control was apparent. This effect could be related to a natural decrease in dentin hypersensitivity over time, or because of patient perception of a decrease in symptoms by virtue of participation in a clinical trial, or may be due to placebo products actually providing some degree of relief from dentin hypersensitivity.[11]

On clinical evaluation, the dentifrice containing 5% NovaMin tested in this study was shown to be significantly efficacious by all three evaluation methods when compared with the potassium nitrate dentifrice and the negative control after two and four weeks of product use. Qualitative results of the companion *in vitro* study showed the test dentifrice containing NovaMin to have tubule occluding properties, while neither the potassium nitrate nor the negative control dentifrices were found to occlude dentin tubules. This is not surprising given that potassium nitrate is a well-established desensitizing ingredient which acts by the release of potassium ions that alter neural transmission at the dentino-pulpal junction.[12] This is unlike NovaMin that acts by tubule occlusion. The results of the SEM companion study are also consistent with those of a series of *in vitro* studies conducted outside of our laboratories that have used SEM with quantification to demonstrate that NovaMin, applied as a slurry to dentin discs, results in significantly more tubule occlusion when compared to an untreated control and to a known tubule occluder (Quell™).[13] The clinical study reported here was not designed to directly compare the onset of effects of 5% NovaMin versus potassium nitrate. It is, however, reasonable to speculate that the observation that Group B (5% NovaMin, test dentifrice) achieved statistically significant reductions in sensitivity compared to baseline after two weeks of product use while Group A (5% potassium nitrate) did not, may be related to the different mechanisms of action of the two active ingredients tested in this study.

Participants' subjective assessment of pain reduction over the treatment period for all three dentifrices mirrored results from the clinical evaluations of product efficacy, thus demonstrating the direct relationship between objective (clinical) and subjective

measurements. This relationship is not wholly unexpected, given that both types of assessments ultimately rely on participants communicating the level of pain they experience. However, it should be noted that the clinical measurements of product efficacy are based on pain experienced at a single point in time in response to specific stimuli applied by the clinician, while the subjective assessment measures the level of "real life" pain each participant recalls experiencing during the period between examinations.[11]

Conclusions

The results of this study compare favorably with those of similar studies performed at higher concentrations of NovaMin (7.5%) elsewhere in India,[6] pilot studies performed in the United States,[14] and at a similar concentration of NovaMin (5.0%) in China[7] and India.[8] These studies have compared dentifrices containing NovaMin to dentifrices without additional desensitizing ingredients, and to products containing active ingredients, such as potassium nitrate, strontium chloride, and stannous fluoride, indicated for the treatment of dentin hypersensitivity. Similar to the findings of our study, NovaMin dentifrices were found to be highly effective in relieving dentin hypersensitivity, often providing superior reduction of dentin hypersensitivity compared to dentifrices without desensitizing ingredients, as well as positive control dentifrices containing recognized desensitizing ingredients, such as potassium nitrate and strontium chloride.

Taken together, the results of these studies support the conclusion that the mode of action of NovaMin leads to a dentifrice which provides clinical relief of dentin hypersensitivity.

Acknowledgment: This study was supported by Group Pharmaceuticals Limited, Mumbai, India. Publication was supported by GlaxoSmithKline Consumer Healthcare.

For further correspondence with the authors of this paper, please contact Dr. Sudhindra Kulkarni—drsudhindrak@gmail.com.

References

1. Holland GR, Narhi MN, Addy M, Gangarosa L, Orchardson R. Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *J Clin Periodontol* 1997;24:808-813.
2. Brännström M, Aström A. The hydrodynamics of the dentine; its possible relationship to dentinal pain. *Int Dent J* 1972;22:219-227.
3. Brännström M, Garberoglio R. The dentinal tubules and the odontoblast processes: A scanning electron microscopic study. *Acta Odontol Scand* 1972;30:291-311.
4. Brännström M. The hydrodynamic theory of dentinal pain: sensation in preparations, caries, and the dentinal crack syndrome. *J Endod* 1986;12:453-457.
5. Yoshiyama M, Masada J, Uchida A, Ishida H. Scanning electron microscopic characterization of sensitive vs. insensitive human radicular dentin. *J Dent Res* 1989;68:1498-1502.
6. Sharma N, Roy S, Kakar A, Greenspan D, Scott R. A clinical study comparing oral formulations containing 7.5% calcium sodium phosphosilicate (NovaMin), 5% potassium nitrate, and 0.4% stannous fluoride for the management of dentin hypersensitivity. *J Clin Dent* 2010;21(Spec Iss):88-92.
7. Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J, Tai BJ. Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (NovaMin) for the treatment of dentin hypersensitivity. *Am J Dent* 2008; 21:210-214.
8. Pradeep AR, Sharma A. Comparison of the clinical efficacy of a dentifrice containing calcium sodium phosphosilicate with a dentifrice containing potassium nitrate and a placebo on dentinal hypersensitivity: A randomized clinical trial. *Periodontol* 2010;81:1167-1173.
9. Addy M. Dentine hypersensitivity: definition, prevalence, distribution and aetiology. In: *Tooth Wear and Sensitivity*, Addy M, Embery G, Edgar WM, Orchardson R, eds. Martin Dunitz Ltd, London, pp. 239-248, 2000.
10. Cummins D. Dentin hypersensitivity: From diagnosis to a breakthrough therapy for everyday sensitivity relief. *J Clin Dent* 2009;20(Spec Iss):1-9.
11. Clark GE, Troullos ES. Designing hypersensitivity clinical studies. *Dent Clin North Am* 1990;34:531-544.
12. Markowitz K. The original desensitizers: strontium and potassium salts. *J Clin Dent* 2009;20(Spec Iss):145-151.
13. Burwell A, Jennings D, Muscle D, Greenspan DC. NovaMin and dentin hypersensitivity—*In vitro* evidence of efficacy. *J Clin Dent* 2010;21(Spec Iss):66-71.
14. Litkowski L, Greenspan DC. A clinical study of the effect of calcium sodium phosphosilicate on dentin hypersensitivity – Proof of principle. *J Clin Dent* 2010;21(Spec Iss):77-81.

A Clinical Study Comparing Oral Formulations Containing 7.5% Calcium Sodium Phosphosilicate (NovaMin®), 5% Potassium Nitrate, and 0.4% Stannous Fluoride for the Management of Dentin Hypersensitivity

Neeru Sharma, BDS, MDS Subrata Roy, MDS Ajay Kakar, BDS, MDS

Armed Forces Medical Center
Pune, India

David C. Greenspan, PhD

Spinode Consulting
Gainesville, FL, USA

Randy Scott

NovaMin Technology Inc.
Alachua, FL, USA

Abstract

- **Objective:** To determine and compare the clinical performance of formulations containing 7.5% calcium sodium phosphosilicate (NovaMin®), 5% potassium nitrate, and 0.4% stannous fluoride for the management of dentin hypersensitivity.
- **Methods:** This was a single-center, randomized, double-blind, parallel-group design with a duration of 12 weeks. The study included a total of 120 subjects and measured sensitivity to cold water and air blast by the use of a visual analogue scale. Measurements were taken at baseline, two, four, and 12 weeks.
- **Results:** All three products significantly reduced sensitivity versus baseline at each time point, although the calcium sodium phosphosilicate (NovaMin) dentifrice reduced sensitivity significantly more than the others at the two- and four-week time points. At the two-week time point, for air and water, respectively, the dentifrice containing NovaMin reduced sensitivity 45% and 49%, the stannous fluoride gel 30% and 26%, and the potassium nitrate dentifrice 35% and 34%. At the 12-week time point, the dentifrice containing NovaMin reduced sensitivity 87% and 91%, stannous fluoride gel 87% and 85%, and potassium nitrate dentifrice 84% and 79%.
- **Conclusion:** In this study, all three products were effective. Compared to the potassium nitrate and stannous fluoride formulations, the dentifrice containing NovaMin provided more substantial and significant improvements at the early time points.

(J Clin Dent 2010;21[Spec Iss]:88–92)

Introduction

Dentin hypersensitivity is a common problem worldwide, affecting as much as 57% of the general population, depending on the locale and population studied.[1-4] The problem peaks in the third decade, but can be an issue at any age.[2] The condition impacts quality of life by reducing dietary options and generally causing pain and discomfort. It may also reduce daily dental hygiene compliance because of pain during brushing or other forms of oral care. New approaches to managing the problem, therefore, can offer patients and clinicians significant advantages.

The commonly held theory on the cause of most sensitivity is the hydrodynamic theory first proposed by Gysi,[5] further described by Brännström and colleagues,[6,7] and confirmed in subsequent work by investigators such as Absi, *et al*.[8] This theory holds that movement of fluids by capillary action in the dentin tubules stimulates receptors in the dentinal pulp, thereby causing pain. Successful approaches to management include potassium ion releasers which depolarize the nerve, eliminating the sensation of pain, and others which can occlude the tubules, preventing a stimulus from inducing fluid movement and leaving the nerve function unaffected. Occluding compounds used and studied in the past include various strontium compounds, stannous fluoride, kaolin, and various oxalates.[9-12]

Nerve depolarizers, such as potassium compounds, have been shown to be effective clinically.[13] Tubule occluders, such as stannous fluoride, have also been shown to be clinically effective,[14-23] although they have been associated with tooth staining and/or bad taste,[24] both of which could potentially reduce compliance. Described in detail in Greenspan,[25] NovaMin® (NovaMin Technology Inc., Alachua, FL, USA) is technically an inorganic, amorphous calcium sodium phosphosilicate (CSPS). It was originally developed as a bone regenerative material, and recently has been engineered for oral care applications. The material has been shown *in vitro* to occlude dentin tubules, and is hypothesized to form a mechanically strong hydroxyl apatite layer on the dentin surface which can resist degradation by repeated acid challenges.[26-28] The purpose of this clinical study was to evaluate the effectiveness of three commercially available products for the treatment of dentin hypersensitivity: a 5% potassium nitrate dentifrice (a nerve depolarizer, positive control); a 0.4% stannous fluoride gel (a known tubule occluder, positive control); and a 7.5% CSPS-containing dentifrice (NovaMin, a new occluding technology, test dentifrice).

Materials and Methods

Study Design

The study was single-center, randomized, double- blind, parallel-group design, with a duration of 12 weeks. The study included 120 subjects, and the protocol followed the guidelines for the design and conduct of clinical trials on dentin hypersensitivity.

The protocol was approved by the Ethics Committee of the medical center. Patients with a history of tooth hypersensitivity, who were seeking treatment in the out-patient dental department of the Armed Forces Medical Centre (Pune, India), were selected for the study with the following inclusion and exclusion criteria.

Inclusion Criteria. Patients were required to be between the ages of 20 and 50 years, in good general health, have at least 20 natural permanent teeth, and a history of hypersensitivity to hot, cold, or sour stimuli on at least two teeth anterior to the molars. Equal numbers of male and female subjects were selected. All patients were evaluated to insure that they were currently using a toothbrush and toothpaste for their oral hygiene procedures.

Exclusion Criteria. Patients with active cervical caries or deep abrasion requiring class V filling, chipped teeth or fractured cusps were excluded from the study. In addition, a tender tooth in the same quadrant as the hypersensitive teeth, and those patients using any type of desensitizing paste or any desensitizing therapy for the prior six months were excluded. Subjects with a history of chronic use of anti-inflammatory and analgesic medication, pregnant or lactating females, those with a history of chronic regurgitation of acids, or who have undergone periodontal surgery in the preceding six months, and those with any denture or bridge work that would interfere with the evaluation of hypersensitivity were also excluded.

Evaluation of Sensitivity

The study was explained to the subjects, and informed consent forms for their willingness to be a part of the study for 12 weeks were obtained. The teeth reported by the subjects to be sensitive were verified by light strokes of a dental explorer along the cervical areas of all teeth present following enrollment in the study. All subjects underwent an oral prophylaxis with an ultrasonic scaler before the study. After a four-week wash-out phase, baseline dentin hypersensitivity levels to cold water and air blast stimuli were measured using a 10 cm visual analogue scale (VAS: 0 = no pain to 10 = severe pain). The facial surfaces of sensitive canines, incisors, and premolars were included. A mean sensitivity score was calculated for each patient using the stimuli. These mean sensitivity scores became the data that were ultimately analyzed.

Air Blast Method. Air from a standard air/water syringe with restricted air stream was directed toward the sensitive portion of the tooth, perpendicular to the long axis of the tooth, for a duration of one second and at a distance of about 0.5 cm. A pressure of 60 psi was selected with the help of a pneumatic pressure control valve. Adjacent teeth were protected by the operator's fingers and cotton rolls. The patient indicated the intensity of pain on the VAS. The test was repeated three times before a score was noted. Teeth with a VAS score of between four and 10 cm were selected.

Cold Water Method. The cold water test was performed approximately 10 minutes after the air blast test. The tooth reported to be sensitive by the patient was isolated with cotton rolls. The cold water stimulus was delivered as one ml of freshly melted ice cold water, applied immediately to the buccal cervical region using an Eppendorf micropipette (Eppendorf Co., Cambridge, UK). The patient indicated the intensity of their pain on the 10 cm VAS. The test was repeated three times before a score was noted. Those teeth with a VAS score between four and 10 cm were selected.

Formulations Tested

Three products, each containing one of the following three components as an active agent, were used:

1) 5% potassium nitrate—Sensodent K, Indoco Remedies Ltd, Warren Pharmaceuticals, Mumbai, India;
2) 0.4% stannous fluoride—Colgate® Gel-Kam®, Colgate-Palmolive (India) Ltd., Mumbai, India; and
3) 7.5% calcium sodium phosphosilicate (NovaMin®)—Soothe Rx™, NovaMin Technology, Inc., Alachua, FL, USA.

After the collection of the baseline data, the subjects were stratified on the basis of gender, and then a subject from each stratum was randomly selected and assigned to each of the treatment groups. The result was three balanced groups, each with 40 subjects and an equal number of males and females. Each group was designated A, B, or C, and based on random choice, assigned to one of the products. In order to maintain the double-blind nature of the study, the products were dispensed in blank white coded tubes by a third party so neither the examiner making clinical assessments nor the patient knew the content. Each patient was provided with an adult soft-bristle toothbrush, and was advised to put about half an inch of product on the brush. Patients were instructed to brush their teeth according to the instructions they were given following prophylaxis for about two minutes, twice daily, with their respective product. The patients were instructed to not eat or drink anything within a half hour of brushing. The patients were recalled at two weeks, four weeks, and 12 weeks for the measurement of tooth sensitivity by the cold water test and the air blast method. At the recall visit, all used product was returned and new material was dispensed. During the study period, patients were prohibited from using other oral hygiene products, other dental treatments for sensitive teeth, and drugs, such as analgesics, which might influence pain perception within 24 hours of assessment days.

Safety

The oral soft tissues were examined at every visit. Subjects were also given the opportunity to report any adverse experiences at any time.

Statistical Methods

ANOVA was performed to determine if there were significant differences in age, baseline air sensitivity, or baseline water sensitivity among the treatment groups. Paired t-tests were performed for each group to compare sensitivity to air and water at time points two, four, and 12 weeks to baseline. ANCOVA

analysis of the group effects at each time point was conducted. A Tukey *post hoc* pair-wise comparison was carried out to determine differences between groups at each time point, using $p < 0.05$ as a significance level. All analyses were performed using Sigma Stat and Sigma Plot 9.0.

Results

Baseline Demographics and VAS Scores

Demographics and baseline VAS scores are displayed in Table I. Stratified assignment by gender was successful; there were 20 males and 20 females in each group. No significant differences in age, baseline air VAS scores, or baseline cold water VAS scores were found among the three treatment groups.

Table I
Baseline Demographics and VAS Scores

	5% Potassium Nitrate Dentifrice	0.4% Stannous Fluoride Dentifrice	7.5% CSPS (NovaMin) Dentifrice
Total Number of Subjects	40	40	40
Male	20	20	20
Female	20	20	20
Mean Age (yrs)	32.0	30.7	32.4
Mean (std dev) Air VAS at Baseline (cm)	5.85 (1.03)	5.83 (1.01)	5.73 (0.99)
Mean (std dev) Cold Water VAS at Baseline (cm)	5.78 (1.12)	5.68 (1.05)	5.60 (0.98)

Note: Group differences at baseline were not statistically significant.

Efficacy

Paired t-tests for each group were conducted comparing sensitivity (unadjusted mean score) for water and air at time points two, four, and 12 weeks to baseline. All products significantly reduced sensitivity compared to baseline for both water and air tests, and there was a clear trend for increasing reductions in sensitivity over time (Tables II and III).

Table II
Air Blast
Mean ± Std Dev VAS Scores in Centimeters
(% Reduction from Baseline)

Time Point	5% Potassium Nitrate Dentifrice	0.4% Stannous Fluoride Dentifrice	7.5% CSPS (NovaMin) Dentifrice
2 Weeks	3.80 ± 1.32 (35%)	4.10 ± 1.13 (30%)	3.15 ± 0.92 (45%)
4 Weeks	2.98 ± 0.80 (49%)	3.18 ± 1.01 (45%)	1.80 ± 0.91 (69%)
12 Weeks	0.95 ± 0.88 (84%)	0.75 ± 0.93 (87%)	0.73 ± 0.78 (87%)

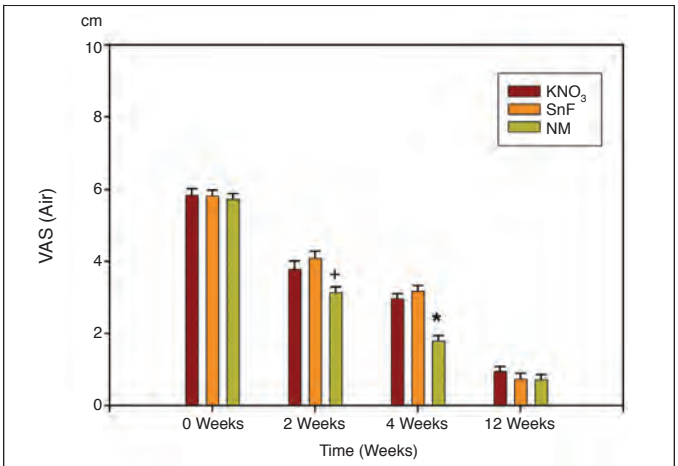
Note: Analysis based on unadjusted means. All within-group pair-wise comparisons to baseline were statistically significant ($p < 0.001$).

ANCOVAs and *post hoc* Tukey pair-wise comparisons were used to analyze for differences among the products in VAS scores for water and air at time points two, four, and 12 weeks. In all ANCOVAs, the effect of baseline was significant at $p < 0.001$, therefore it was used as the covariate. The results are shown in Figures 1 and 2. There was a significant statistical

Table III
Cold Water
Mean ± Std Dev VAS Scores in Centimeters
(% Reduction from Baseline)

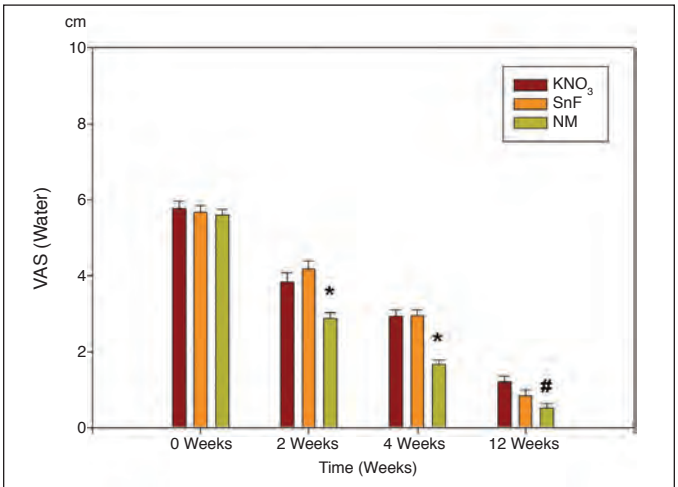
Time Point	5% Potassium Nitrate Dentifrice	0.4% Stannous Fluoride Dentifrice	7.5% CSPS (NovaMin) Dentifrice
2 Weeks	3.83 ± 1.57 (34%)	4.18 ± 1.38 (26%)	2.88 ± 0.91 (49%)
4 Weeks	2.93 ± 1.10 (49%)	2.95 ± 0.99 (48%)	1.68 ± 0.66 (70%)
12 Weeks	1.20 ± 0.97 (79%)	0.85 ± 0.86 (85%)	0.53 ± 0.68 (91%)

Note: Analysis based on unadjusted means. All within-group pair-wise comparisons to baseline were statistically significant ($p < 0.001$)



*Significant reduction in sensitivity ($p < 0.05$) when compared to KNO_3 and SnF.
†Significant reduction in sensitivity ($p < 0.05$) when compared to SnF.
Note: Analysis for group effect based on 1s mean using ANCOVA with baseline as covariate. Within-group analysis using Tukey *post hoc* pair-wise comparison.

Figure 1. *Mean sensitivity scores following challenge with an air blast (VAS: 0 = no pain; 10 = severe pain).*



*Significant reduction in sensitivity ($p < 0.05$) when compared to KNO_3 and SnF.
#Significant reduction in sensitivity ($p < 0.05$) when compared to KNO_3.
Note: Analysis for group effect based on 1s mean using ANCOVA with baseline as covariate. Within-group analysis using Tukey *post hoc* pair-wise comparison.

Figure 2. *Mean sensitivity scores following a challenge with cold water (VAS: 0 = no pain; 10 = severe pain).*

group effect at weeks two and four among the air VAS scores. Based on pair-wise comparisons, use of the CSPS (NovaMin) dentifrice was more effective than either positive control product, *i.e.*, the stannous fluoride gel or potassium nitrate dentifrice. There was no significant statistical difference between the use of the stannous fluoride gel and potassium nitrate dentifrice. There were no significant statistical differences in air VAS scores among the three treatment groups at week 12. Analysis of the VAS scores for water at weeks two and four indicates that the NovaMin dentifrice was more effective than either the stannous fluoride gel or the potassium nitrate dentifrice. For water at week 12, there was a significant main effect for the group, with NovaMin being more effective than either the stannous fluoride gel or the potassium nitrate dentifrice.

Safety

All patients completed the study and there were no adverse events reported during the study for any of the products used.

Discussion

The objective of this study was to evaluate and compare, in an Indian population, the efficacy of three commercially available products, each containing one of the following ingredients for the treatment of dentin hypersensitivity: 5% potassium nitrate; 0.4% stannous fluoride; or 7.5% CSPS (NovaMin).

Potassium, a well-established and researched ingredient, was recently reviewed by Markowitz.[9] Potassium nitrate is an inorganic salt found in contemporary desensitizing products. In preclinical studies, the potassium ion has been shown to be the active component of potassium nitrate that exerts an inhibitory action on the intradental nerves. Other potassium compounds, such as potassium chloride, potassium citrate, and potassium bicarbonate, were also found to depress nerve excitability. In clinical trials of dentifrices containing potassium nitrate, pain reduction increases with the duration of dentifrice use and, in general, two or more weeks of twice-daily use of the dentifrice are required before significant pain reduction is observed. Potassium nitrate has been recognized as safe and effective for the treatment of dentin hypersensitivity by the United States Food and Drug Administration.[29]

Stannous fluoride is a clinically proven ingredient used in toothpastes[23,24] and topically applied gels[19-22] for the treatment of dentin hypersensitivity. Results of clinical studies of products containing stannous fluoride have shown efficacy following two to four weeks of twice-daily application.

The use of CSPS (NovaMin) in a dentifrice is a relatively new approach to tubule occlusion. There is a significant amount of *in vitro* data that indicates its potential as a remineralizing and desensitizing agent,[30] as well as a growing body of evidence to support its clinical efficacy. The technology is based on the potential of CSPS to remineralize tooth structure by increasing salivary calcium and phosphate levels and, in some cases, increasing the salivary pH, resulting in the formation of calcium phosphate or hydroxyapatite.[31] In laboratory studies, NovaMin has been shown to very rapidly occlude dentin tubules and thought to form a hydroxyapatite layer that can resist degradation by repeated acid challenges.[32]

In the present study, significant reductions in VAS scores at the two-week time point, as well as subsequent time points measured after baseline, were observed, indicating all three products effectively reduce sensitivity when applied twice daily. No differences were observed between the potassium and stannous fluoride products, indicating that both exhibit similar efficacy. However, compared to products containing potassium or stannous fluoride, the reduction of sensitivity associated with the use of a dentifrice containing NovaMin is significantly greater after two weeks of twice-daily use. By the 12-week assessment, however, the air scores for all three product groups were similar. This may be due to a floor effect; that is, the use of NovaMin results in a rapid and greater reduction in sensitivity, but at 12 weeks the other products approach similar reductions with no room on the measurement scale to show further improvements. A negative control was not included in this study since both potassium nitrate and stannous fluoride are clinically proven to be effective. In addition, design controls, such as randomization, double-blinding, and standardized application of stimuli, were used to minimize variability and achieve a consistent placebo response across all three treatment groups.[33,34] Therefore, the more substantial effects of NovaMin dentifrice at the early time points are not due solely to placebo effects .

Conclusion

In this study, all three products were effective. Compared to the potassium nitrate and stannous fluoride formulations, the dentifrice containing NovaMin provided more substantial and significant improvements at early time points. The results of this study are in accord with other studies of dentifrices containing 7.5% CSPS (NovaMin) conducted in the United States[35] and India,[36-38] as well as more recent studies with 5.0% CSPS in China,[3] which support the conclusion that the use of a dentifrice containing NovaMin leads to clinical relief of dentin hypersensitivity.

Acknowledgments: This study was completed in partial fulfillment of Major Neeru Sharma's post-graduate study requirements. The authors wish to thank NovaMin Technology Inc. for supplying the Soothe Rx toothpaste in unbranded, blank white tubes for use in the study. Preparation of this manuscript was funded by a grant from NovaMin Technology Inc., Alachua, Florida, USA. Publication of this study was supported by GlaxoSmithKline Consumer Healthcare.

For further correspondence with the authors of this paper, please contact Dr. David Greenspan—dspinode@gmail.com.

References

1. Chabanski MB, Gillam DG. Aetiology, prevalence and clinical features of cervical dentine sensitivity. *J Oral Rehabil* 1997;24:15-19.
2. Dababneh RH, Khouri AT, Addy M. Dentine hypersensitivity- an enigma? A review of terminology, mechanisms, aetiology and management. *Br Dent J* 1999;187:606-611.
3. Liu HC, Lan WH, Hsieh CC. Prevalence and distribution of cervical dentin hypersensitivity in a population in Taipei, Taiwan. *J Endod* 1998;24:45-47.
4. Chabanski MB, Gillam DG, Bulman JS, Newman HN. Clinical evaluation of cervical dentine sensitivity in a population of patients referred to a specialist periodontology department: a pilot study. *J Oral Rehabil* 1997;24:666-672.
5. Gysi A: An attempt to explain the sensitiveness of dentin. *Br J Dent Sci* 1900;43:865-868.
6. Brännström M. The hydrodynamic theory of dentinal pain: sensation in preparations, caries and the dentinal crack syndrome. *J Endod* 12:453-457.
7. Brännström M, Lindén LA, Aström A. The hydrodynamics of the dental tubule and of pulp fluid. A discussion of its significance in relation to denti-

nal sensitivity. *Caries Res* 1967;1:310-317.
8. Absi EG, Addy M, Adams D. Dentine hypersensitivity: the development and evaluation of a replica technique to study sensitive and non-sensitive cervical dentine. *J Clin Periodontol* 1989;16:190-195.
9. Markowitz K. The original desensitizers: strontium and potassium salts. *J Clin Dent* 2009;20(Spec Iss):145-151.
10. Orchardson R. Strategies for the management of dentine hypersensitivity. In: *Tooth Wear and Sensitivity*, Addy M, Embery G, Edgar WM, Orchardson R, eds. Martin Dunitz Ltd, London, pp. 315-325, 2000.
11. Kanapka JA. Over-the-counter dentifrices in the treatment of tooth hypersensitivity: Review of clinical studies. *Dent Clin North Am* 1990;34:545-560.
12. Trowbridge HO, Silver DR. A review of current approaches to in-office management of tooth hypersensitivity. *Dent Clin North Am* 1990;34:561-581.
13. Orchardson R, Gillam DG. The efficacy of potassium salts as agents for treating dentin hypersensitivity. *J Orofac Pain* 2000;14:9-19.
14. Kobler A, Kub O, Schaller HG, Gernhardt CR. Clinical effectiveness of a strontium chloride-containing desensitizing agent over 6 months: A randomized, double-blind, placebo-controlled study. *Quintessence Int* 2008;39:321-325.
15. West NX, Addy M, Jackson RJ, Ridge DB. Dentine hypersensitivity and the placebo response: A comparison of the effect of strontium acetate, potassium nitrate and fluoride toothpastes. *J Clin Periodontol* 1997;24:209-215.
16. Minkoff S, Axelrod S. Efficacy of strontium chloride in dental hypersensitivity. *J Periodontol* 1987;58:470-474.
17. Addy M, Mostafa P, Newcombe R. Dentine hypersensitivity: A comparison of five toothpastes used during a 6-week treatment period. *Br Dent J* 1987;163:45-51.
18. Uchida A, Wakano Y, Fukuyama O, Miki T, Iwayama Y, Okada H. Controlled clinical evaluation of a 10% strontium chloride dentifrice in treatment of dentin hypersensitivity following periodontal surgery. *J Periodontol* 1980;51:578-581.
19. Thrash WJ, Dodds MW, Jones DL. The effect of stannous fluoride on dentinal hypersensitivity. *Int Dent J* 1994;44(Suppl 1):107-118.
20. Blong MA, Volding B, Thrash WJ, Jones DL. Effects of a gel containing 0.4 percent stannous fluoride on dentinal hypersensitivity. *Dent Hyg* 1985;59: 489-492.
21. Miller JT, Shannon IL, Kilgore WG, Bookman JE. Use of a water-free stannous fluoride-containing gel in the control of dental hypersensitivity. *J Periodontol* 1969;40:490-491.
22. Schiff T, He T, Sagel L, Baker R. Efficacy and safety of a novel stabilized stannous fluoride and sodium hexametaphosphate dentifrice for dentinal hypersensitivity. *J Contemp Dent Pract* 2006;7:1-8.
23. Schiff T, Saletta L, Baker RA, Winston JL, He T. Desensitizing effect of a stabilized stannous fluoride/sodium hexametaphosphate dentifrice. *Compend Contin Educ Dent* 2005;26(Suppl 1):35-40.
24. Tinanoff N. Progress regarding the use of stannous fluoride in clinical dentistry. *J Clin Dent* 1995;6(Spec Iss):37-40.
25. Greenspan DC. NovaMin® and tooth sensitivity- An overview. *J Clin Dent* 2010;21(Spec Iss):61-65.
26. Jennings DT, McKenzie KM, Greenspan DC, Clark AE. Quantitative analysis of tubule occlusion using NovaMin® (sodium calcium phosphosilicate). *J Dent Res* 2006;83(Spec Iss C):2416.
27. Burwell A, Greenspan DC. Quantitative tubule occlusion in an *in vitro* remineralization/demineralization model. *J Dent Res* 2006;85(Spec Iss C):568.
28. Litkowski LJ, Hack GD, Sheaffer HB, Greenspan DC. Occlusion of dentin tubules by 45S5 Bioglass®. In: *Bioceramics 10, Proceedings of the 10th International Symposium on Ceramics in Medicine*, Paris, France. Sedel L, Rey C, eds., 1997.
29. United States Department of Health and Human Services Food and Drug Administration. *Federal Register* 1991;56:48308-43810.
30. Wefel JS. NovaMin: likely clinical success. *Adv Dent Res* 2009;21:40-43.
31. LaTorre G, Greenspan DC. The role of ionic release from NovaMin (calcium sodium phosphosilicate) in tubule occlusion: An exploratory *in vitro* study using radio-labeled isotopes. *J Clin Dent* 2010;21(Spec Iss):72-76.
32. Greenspan DC. NovaMin and tooth sensitivity—An overview. *J Clin Dent* 2010:61-65.
33. Curro FA. Tooth hypersensitivity in the spectrum of pain. *Dent Clin North Am* 1990;34:429-437.
34. Curro FA, Friedman M, Leight RS. Design and conduct of clinical trials on dentin hypersensitivity. In: *Tooth Wear and Sensitivity*, Addy M, Embery G, Edgar MW, Orchardson R, eds. Martin Dunitz Ltd., London, 2000, pp. 299-314.
35. Litkowski L, Greenspan DC. A clinical study of the effect of calcium sodium phosphosilicate on dentin hypersensitivity—Proof of principle. *J Clin Dent* 2010;21(Spec Iss):77-81.
36. Salian S, Thakur S, Kulkarni S. A randomized controlled clinical study evaluating the efficacy of two desensitizing dentifrices. *J Clin Dent* 2010; 21(Spec Iss):82-87.
37. Pradeep AR, Sharma A. Comparison of clinical efficacy of a dentifrice containing calcium sodium phosphosilicate to a dentifrice containing potassium nitrate and to a placebo on dentinal hypersensitivity: A randomized clinical trial. *J Periodontol* 2010;81:1167-1173.
38. Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J, Tai BJ. Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (novamin) for the treatment of dentin hypersensitivity. *Am J Dent* 2008;21:210-214.

Instructions for Authors
The Journal of Clinical Dentistry

Mission Statement—*The Journal* is dedicated to the rapid publication of research and reviews focused on preventive oral healthcare products and new dental materials. Both laboratory and clinical research are accepted, as well as case reports. All scientific studies are blinded and peer-reviewed by an expert panel of researchers at independent academic institutions. *The Journal* also publishes issues dedicated to a single product and its research and development. These publications are designed to educate the dental professional on the safety and efficacy of these products so an informed and confident product recommendation can be made to patients. *The Journal* accepts no advertising. ***All papers accepted for publication will be assessed a placement fee of US$800 per published page.***

Manuscript Submission—All manuscripts are to be previously unpublished, in whole or in part, to be acceptable for review and publication. *The Journal* will be assigned all rights to works accepted for publication. Manuscripts, figures, and tables should be prepared in either Word or WordPerfect, and emailed as an attachment to EditorJCD@AOL.COM. All manuscripts should be double-spaced and composed of the following sections: Abstract (Objective, Methods, Results, Conclusions), Introduction (with background of prior research and problem statement), Materials and Methods (how the research was conducted specifically), Results (with data and findings only), Discussion (author description of meaning of the results, conclusions, and directions for future research in the area), and References (formats listed below). Additionally, *The Journal* requires disclosure of the source for funding of the study, if any, in an Acknowledgment to appear at the end of the paper. The corresponding author will be identified, with e-mail address, following the Acknowledgment.

Manuscript Format—The following format applies to manuscripts; those which do not follow the format will be returned for adjustments.

- Abstracts are brief and are used only as a summary of the research.
- Tables are numbered using Roman notation (*e.g.*, I, II, III, IV, etc.) with centered titles and initial caps.
- Figures are numbered using Arabic notations (*e.g.*, 1, 2, 3, etc.) with descriptions to be placed below the figure.
- All tables and figures are to be referred to within the text to aid the reader.
- All named products should be followed by either a ™ or ®, and should include the product's manufacturer and location of same by city and country within parentheses.
- Indexing is used at the completion of an annual volume. As such, three to ten key words should accompany each paper.
- Author affiliations are encouraged, along with credentials such as DDS, DMD, PhD, etc.

Citations—All previous work or factual statements require documentation from the published literature. Citations should be numbered as they appear within the text and listed by the same number within the Reference section of the paper. For the convenience of the reader, citations in the text may only be listed by reference number, or if reference to the authors is made, only the first author should be listed followed by *et al*. When a citation has just two authors, both names should be cited in the text. All authors of a cited publication MUST BE LISTED within the Reference section of the paper (*et al*. is not accepted in Reference section). The following sample format applies to all references:

Book Source

Whole Book

Smith DF, Jones GH. *Dental Hygiene and Dental Practice*. 3rd Ed. Scientific Publisher, Philadelphia, 2010.

Chapter within Book

Black JK. Root scaling. In: *Dental Hygiene and Dental Practice,* Smith DF, Jones GH, eds. Scientific Publisher, Philadelphia, pp. 325-50, 2010.

Journal Source *(Please note new format)*

White DJ, Duschner H, Pioch T. Effect of bleaching treatments on microleakage of Class I restorations. *J Clin Dent* 2008;19:33-36.

Spelling and syntax used within the manuscript will be corrected using the Random House Dictionary of the English Language (American Version). All numbers in the text of ten or less should be written out (*e.g.*, one, five, ten). All numbers over ten should be given in numeric form (*e.g.*, 11, 15, 116). No abbreviations such as "vs." or "exam" should be used in place of "versus" or "examination."

Following manuscript review, the Senior Editor will compile the comments of the reviewers, along with his own, and correspond with the lead author detailing adjustments which will be required before a paper is considered "accepted." Re-submitted papers are thoroughly reviewed to confirm compliance with the comments.

Following acceptance, page proofs will be forwarded to the lead author for approval and assignment (sign-off). These must be returned as soon as possible to the Publisher with notations or corrections. All papers accepted for publication will be in print within 16 weeks of acceptance.

Contact Information	E-mail	Phone	Fax
Robert C. Emling, Editor	EditorJCD@AOL.COM	+410-708-4980	+775-373-1989
Stephen M. Siegel, Publisher	Dntlpblshr@JClinDent.Com	+215-493-7400	+215-493-9804

The Journal of Clinical Dentistry
is printed on
recycled paper.

Journal section: Biomaterials and bioengineering in dentistry
Publication Types: Research

Ultramorphology and dentine permeability changes induced by prophylactic procedures on exposed dentinal tubules in middle dentine

Salvatore Sauro [1], Timothy F Watson [2], Ian Thompson [3]

[1] BDH, PhD, Biomaterials, Biomimetics & Biophotonics Research Group (B3), King's College London Dental Institute, Guy's, King's College and St Thomas' Hospitals, London, United Kingdom
[2] BSC, BDS, PhD, FDS, professor and chairman, Biomaterials, Biomimetics & Biophotonics Research Group (B3), King's College London Dental Institute, Guy's, King's College and St Thomas' Hospitals, London, United Kingdom
[3] PhD, senior lecturer, Biomaterials, Biomimetics & Biophotonics Research Group (B3), King's College London Dental Institute, Guy's, King's College and St Thomas' Hospitals, London, United Kingdom

Correspondence:
Biomaterials, Biomimetics & Biophotonics
King's College London Dental Institute
Guy's, King's College and St Thomas' Hospitals
Floor 17 Guy's Tower
London, SE1 9RT
England
salvatore.sauro@kcl.ac.uk

Received: 13-11-2010
Accepted: 16-01-2011

Abstract

Objectives: The purpose of this study was to evaluate the changes in dentinal permeability (i.e. hydraulic conductance) after prophylactic treatments performed using prophy-powders with air-polishing system or prophy-pastes on exposed middle dentine. The changes in dentine morphology were evaluated by SEM.

Study design: Commercial prophylactic pastes and air-polishing powders were tested in this study. Dentine discs from human third molars were used to study the quantitative reduction of the dentine permeability under simulated pulpal pressure (20 cm H_2O). Further specimens were gold-coated and analysed using observed a SEM.

Results: The results of this study showed different dentine permeability redaction based on the type of product employed (i.e. prophylactic paste or air-polishing powders). The use of Sylc bioactive glass and sodium bicarbonate were the most effective in reducing dentine permeability of the specimens. However, the air-polishing procedures performed with Sylc bioactive glass created a dentine surface devoid of exposed dentinal tubules due to the presence of a compact multilayered smear layer. Colgate Sensitive Pro-Relief and Nupro NU-Solution reduced the dentine permeability up to 69.8% and 66.9% respectively.

Conclusion: Although all the tested products are able to statistically reduce dentine permeability, Sylc bioactive glass is an innovative and effective product which completely occludes the dentinal tubules during prophylactic procedures of air-polishing.

Key words: *Prophylactic pastes.*

Introduction

The clinical symptoms of dentine hypersensitivity (DH) is commonly reported during the clinical practice, in particular, subsequent to non-surgical periodontal therapy performed with sonic and manual instruments due to the removal of the thin layer of cementum in the cervical region and along the root surface (1-5). Dentine hypersensitivity is also induced by the enamel loss and/or the gingival root surface abrasion caused by the erosion, abfraction or gingival recession (6-7).

The hydrodynamic theory proposed by Brännström *et al*, (8) states that thermal, evaporative, tactile, osmotic or chemical stimuli induce the movement of fluid within open dentine tubules (9, 10). The movement of the intratubular fluid activates mechanoreceptor nerves, eliciting sharp pain and discomfort which may not be ascribed to any other form or dental defect or pathology (8, 9).

Based on the principles of the hydrodynamic theory it has been possible to establish a consistent correlation between fluid flow and the physical occlusion of dentine tubules to evaluate the effects of dentine desensitizes. Indeed, the concept behind this method is that any substance able to obliterate the dentinal tubules and reduce the movement of the intratubular fluid may be suitable for the treatment of DH (8, 10, 11). Air polishing as a prophylaxis technique has become very popular with specialists in preventive dentistry as alternative to rotary-rubber instruments (12-15). Furthermore, these systems might also be used for enamel cleaning prior to pit and fissure sealing or orthodontic bracket bonding and in the treatment of root surfaces during non-surgical periodontal therapy as a valid alternative to hand, sonic and ultrasonic scalers (16, 17).

Although prophylactic measures performed with polishing rubber cup (PRC) or air-polishing systems (AP) showed to be able to reduce the intratubular fluid flow when applied on deep dentine (18), there is little information on the effects of these treatments when applied in different morphological and working parameters.

The purpose of this study was to evaluate the changes in dentinal permeability (i.e. hydraulic conductance) after prophylactic treatment performed using prophy-powders with a 4-bar air-polishing system or prophy-pastes used with PRC applied on exposed middle dentine. The ultra-morphological changes induced by these experimental treatments when applied on middle dentine were evaluated by using scanning electron microscopy (SEM).

Materials and Methods

-Specimen preparation for dentine permeability

Thirty human third molars from patients (aged 20–40 years) which were extracted for surgical reasons were collected and stored in deionised water (pH 7.4) at 4°C for the experiments that were conducted within one month of extraction. Protocols were reviewed and approved by the Ethics Committee of the Academic Health Science Centre at King's College London, including informed consent for tissue use in research. Dentine segments were obtained by first removing the roots 1.5 mm beneath the cementum-enamel junction (CEJ) using a slow-speed water-cooled diamond saw (Labcut, Agar Scientific, Stansted, UK). The occlusal enamel was removed with a parallel cut to expose the middle dentine. Pulpal tissue was carefully removed from the exposed pulp chamber without crushing the pre-dentine surface by using thin tissue forceps. A pincer-type caliper was used for measuring the remaining dentine thickness (RDT) from the surface to the highest pulpal horns (1.2 ± 0.1 mm). Each tooth section was positioned on a Perspex™ platform (2 cm×2 cm×0.5 cm) (Perspex Distributions Ltd., London, UK) that was perforated by an 18 gauge stainless steel tube using cyanocrylate adhesive (ROCKET Heavy DVA, Corona, CA, USA). Each specimen was connected to a hydraulic fluid filtration system able to deliver a simulated pulpal pressure of 20 cm H2O. A modified split-chamber device was used to allow the standardization of exposed dentine area for fluid filtration by using pairs of rubber "O" rings with an internal diameter of 0.6 cm (Area: 0.38 $cm^{2)}$ (Fig. 1). A 25 µL capacity micro-capillary tube (Microcaps, Fisher Scientific, Atlanta, GA, USA) was horizontally positioned between the pressure reservoir and the crown segment (Fig. 1). The linear displacement of an air bubble inside the micro-capillary tube indicated the volume displacement which is converted into a measure of the hydraulic conductance. The linear displacement of the air bubble was converted into volume flow (µL min^{-1}). For each specimen, fluid flow across the dentine discs were then transformed into hydraulic conductance (Lp) (µLmin^{-1} cm^{-2} cm H_2O^{-1}), by dividing the fluid flow (µL min-1) by the exposed dentine surface area (cm^2) and the water pressure (cm H_2O, i.e. 20 cm H_2O) (19, 20).

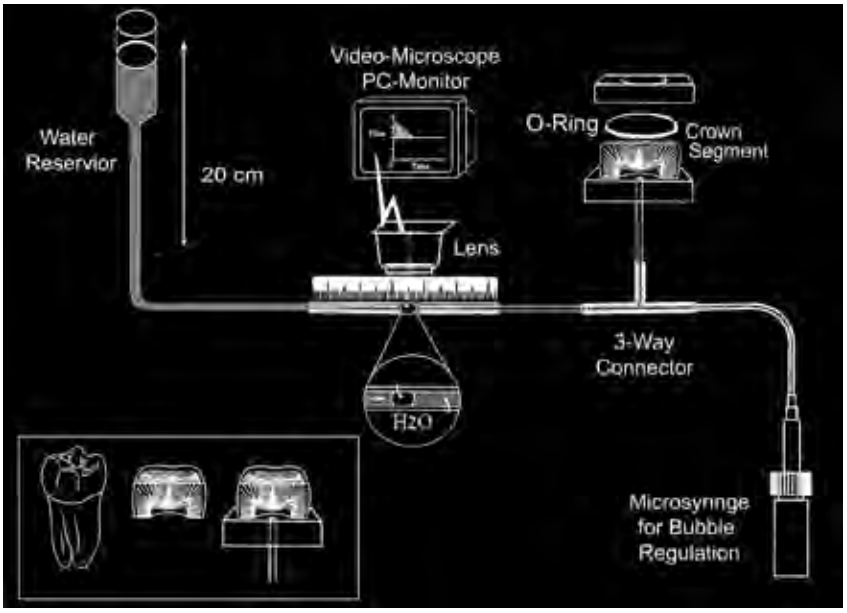


Fig. 1. Scheme depicting the creation of crown segments, the attachment to Perplex and how fluid permeability was measured under 20cm H_2O pressure.

-*Experimental design for dentine permeability*

A homogeneous smear layer was created on each dentine surface using a 320-grit SiC abrasive paper for 25 s. Subsequently, the Lp was measured to evaluate the minimum permeability of each specimen. The smear layer was then removed, treating the dentine surface using 37% orthophosphoric acid solution (H_3PO_4) for 30 sec (PA). Subsequently, the dentine surface was copiously water-rinsed and the Lp was measured in order to obtain the highest permeability (Lp max = 100% was arbitrarily assigned). Lp 100% permits evaluation of modifications in dentinal permeability following the test treatments.

Evaluations of dentine permeability were performed by measurement of convective fluid flow through each crown segment under 20 cm H_2O of water pressure for 3 min in triplicate. This sequence was repeated three times for each specimen and averaged to calculate a single mean value. This mean value was then averaged for all specimens in each treatment group to obtain the dentine permeability (Lp). All treatments were applied on wet dentine surface (18, 20).

The list of products used in this study, the composition and the application mode are shown in Table 1. The air-polishing system (AP) used to jet-spray the different prophy-powders of this study was the Aquacut Quattro (VELOPEX INTERNATIONAL, London, UK) working at air pressure of 4 bar (400 MPa) and a distance of 5 mm.

Statistical analyses were performed using SPSS 16.0 (SPSS Inc. Chicago, IL, USA) program. The means and standard deviations of each group were calculated from Lp% obtained from the treatments. Statistically significant differences were identified among the groups by ANOVA ($P < 0.001$). Fisher's least significant difference (LSD) test was used to isolate and compare the significant differences ($P < 0.05$) between the groups.

-*Scanning electron microscopy (SEM)*

Twelve recently extracted human molars were used for SEM investigation. Dentine slices were obtained from deep-coronal dentine of each tooth using a slow-speed water-cooled diamond saw (Labcut, Agar Scientific, UK). They were randomly divided into 6 groups of 4 slices each for examination with SEM. Dentine slices were polished using a 320 grit SiC abrasive paper to compose a standardized smear layer. The specimens were submitted to the same experimental treatment design as previously described in dentine permeability evaluation section.

The specimens from each group were dried and then mounted on aluminium stubs with carbon cement. They were sputter-coated with gold (SCD 004 Sputter Coater; Bal-Tec, Vaduz, Liechtenstein) and viewed using a scanning electron microscope (SEM) (S-3500; Hitachi, Wokingham, UK) with an accelerating voltage of 15 kV and a working distance of 14 mm at increasing magnifications from 100X to 2500X.

Table 1. Products used in this study, composition and application mode.

Treatments (acronym)	Manufacturing	Components	Application mode
Sylc bioactive glass® Powder	Sylc, OSspray ltd, Cambridge, UK	Bioactive glass (SiO_2, Na_2O, CaO P_2O_5)	Air-polishing operated in a Prophyflex air-polishing device (Velopex) at a distance of 5 mm for 15s.
Sylc bioactive glass® H_2O	Sylc, OSspray ltd, Cambridge, UK	Bioactive glass (SiO_2, Na_2O, CaO P_2O_5) Deionized water	Applied to dentin using a slow-speed handpiece with a prophylaxis angle attachment angle and rotating rubber cup for 30 s
Cavitron® *Prophy-Jet*® *sodium bicarbonate*	Dentslpy corp., London, UK	sodium bicarbonate ($NaHCO_3$)	Air-polishing operated in a Prophyflex air-polishing device (Velopex) at a distance of 5 mm for 15 s.
AIR-flow® powder PERIO	EMS corp., Nyon Swizerland	Amino-acid-glycine	Air-polishing operated in a Prophyflex air-polishing device (Velopex) at a distance of 5 mm for 15 s.
Colgate® Sensitive Pro-Relief™	Colgate Palmolive, New York, NY	Hydrated silica, calcium carbonate, glycerin, 8% arginine, water, bicarbonate, flavor, cellulose gum, sodium saccharin, FD&C blue no. 1 (CI 42090)	Applied to dentin using a slow-speed handpiece with a prophylaxis angle attachment angle and rotating rubber cup for 30 s
NUPRO® NUSolutions™ Prophy Paste	Dentslpy corp., London, UK	Hydrated silica, glycerin, water, bicarbonate, flavor, cellulose gum, sodium saccharin and bioactive glass NovaMin®	Applied to dentin using a slow-speed handpiece with a prophylaxis angle attachment angle and rotating rubber cup for 30 s

Results

The results of this study showed that all the tested products reduced the dentine permeability, compared to the maximum fluid flow of PA-etched dentine (Table 2). The application of 37% H_3PO_4 to the dentine surface caused the exposure of dentinal tubules (Fig. 2.A) and the measure of permeability was arbitrarily considered to be 100%; each H_3PO_4-treated dentine was considered as its own control of specimen after each desensitizing treatment tested in this study (18).

Although Sylc bioactive glass (P% 11.2%) showed statistically higher permeability reduction compared to Prophy-Jet sodium bicarbonate (P% 19.7%), these to prophy-powders resulted significantly most effective than the other treatments. The use of EMS Perio powder applied to exposed dentine induced a reduction of the dentine permeability up to 68.8%. SEM investigation supported the permeability results showing that the air-polishing procedures performed on dentine using Sylc bioactive glass (Fig. 2.B) and bicarbonate (Fig. 2.C) occluded the dentinal tubules by forming a smear layer on the dentine surface.

The dentine surface air-polished using EMS Perio Powder showed the presence of dentinal tubules characterized by an altered morphology and only partially occluded (Fig. 2.D). However, the SEM investigation also showed that some of the tubules remained open (Fig. 4.A). The bioactive glass mixed with water and applied using a rotatory rubber cup reduced the dentine permeability up to 81.1% resulting statistically more effective than the other prophy-pastes; no statistical difference was observed when compared to the permeability reduction induced by sodium bicarbonate applied with the air-polishing device (Table 2).

SEM investigation showed that the use of Sylc bioactive glass/H_2O as prophy-paste was suitable for the occlu-

sion of the dentinal tubules with the formation smear plugs inside the dentinal tubules (Fig. 3.A, 4.B).

Colgate Sensitive Pro-Relief reduced the dentine permeability of the H_3PO_4-treated dentine up to 30.2%. The SEM investigation showed that Colgate Sensitive Pro-Relief was able to reduce the diameter of the lumen of the tubules (Fig. 3.C, 4.C).

NUPRO Solution Prophy Paste reduced the dentine permeability up to 66.9% showing a dentine surface that was partially covered with small smear layer-like debris (Fig. 3.B). However, at higher magnifications it was possible to observe that the dentinal tubules were still open or only partially obliterated (Fig. 4.C).

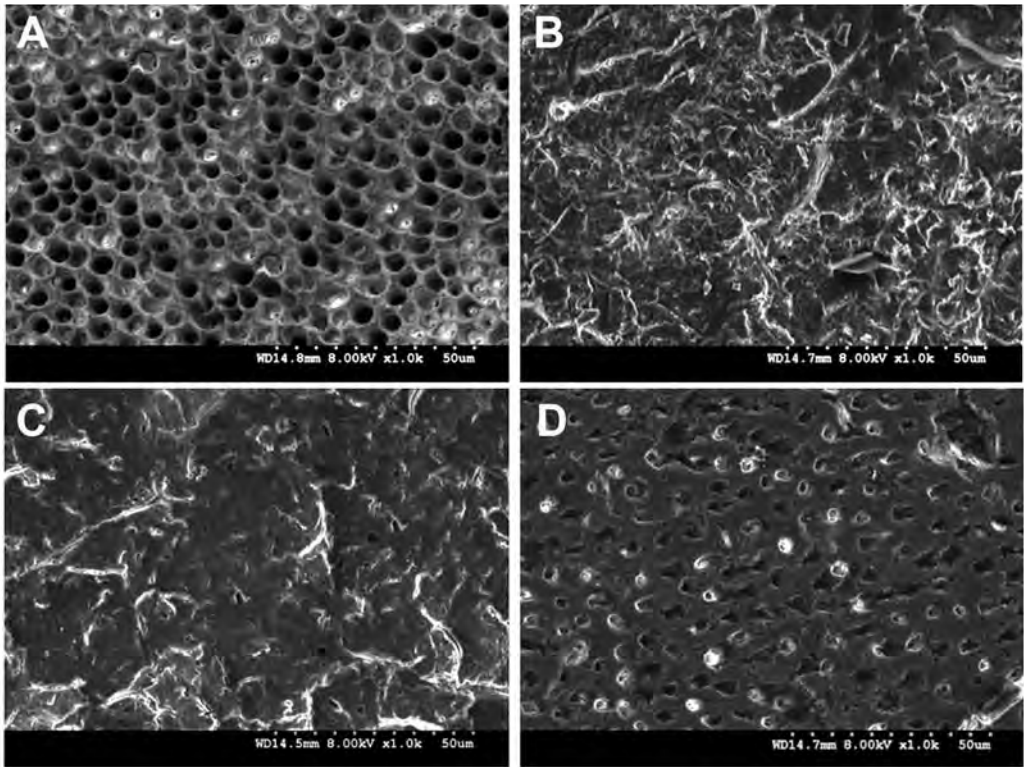


Fig. 2. 1000X SEM micrographs of dentine surfaces air-polished using the prophy-powders tested in this study. **A)** shows the effects of H_3PO_4 on the dentine surface resulting in completely opened dentinal tubules. **B)** shows the effects of Sylc bioactive glass powder on the dentine surface. This procedure creates the multilayered smear layer that occludes the dentinal tubules. The pictures **C)** shows the effects of Prophy-Jet sodium bicarbonate powder on the dentine surface showing how this procedure also created a smear layer that covers the dentine surface and occludes the dentinal tubules. **D)** shows the effects of EMS Perio powder on the dentine surface resulting in completely or partially opened tubules.

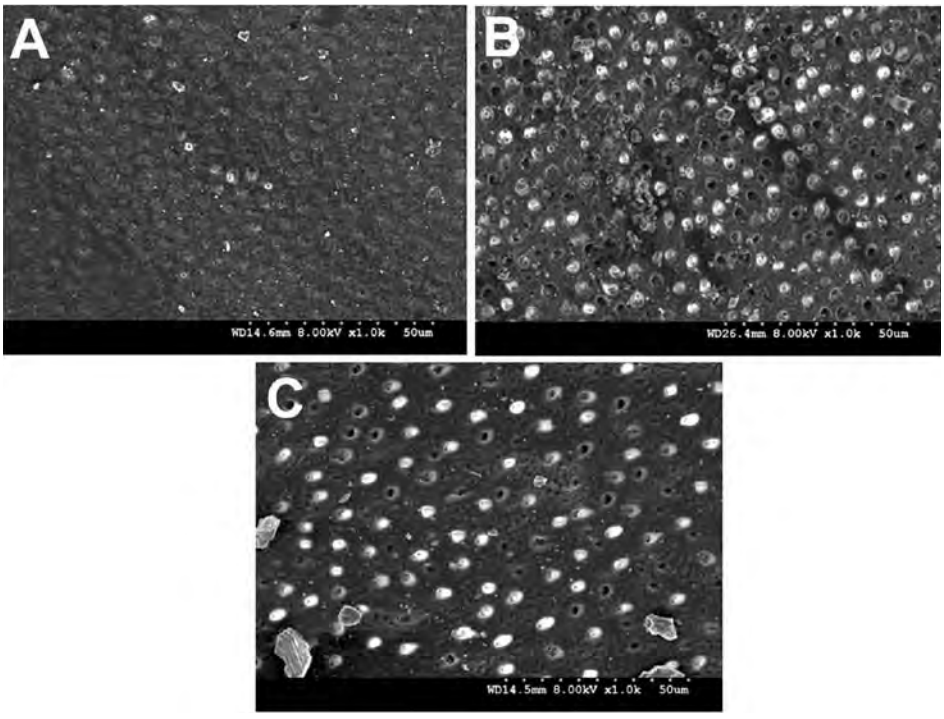


Fig. 3. 1000X SEM micrographs of dentine surfaces treated using the three prophy-pastes tested in this study. Sylc bioactive glass **A)**: the application of this product as prophy paste induced the complete occlusion of most of dentinal tubules leavingthe dentine surface relatively smooth. Nupro Solution Prophy Paste **B)**: the dentine surface appears superficially covered by residual debris that partially or completely occludes the dentinal tubules. Colgate Sensitive Pro-Relief **C)**: the dentine surface appears prevalently smooth with partially occluded dentinal tubules.

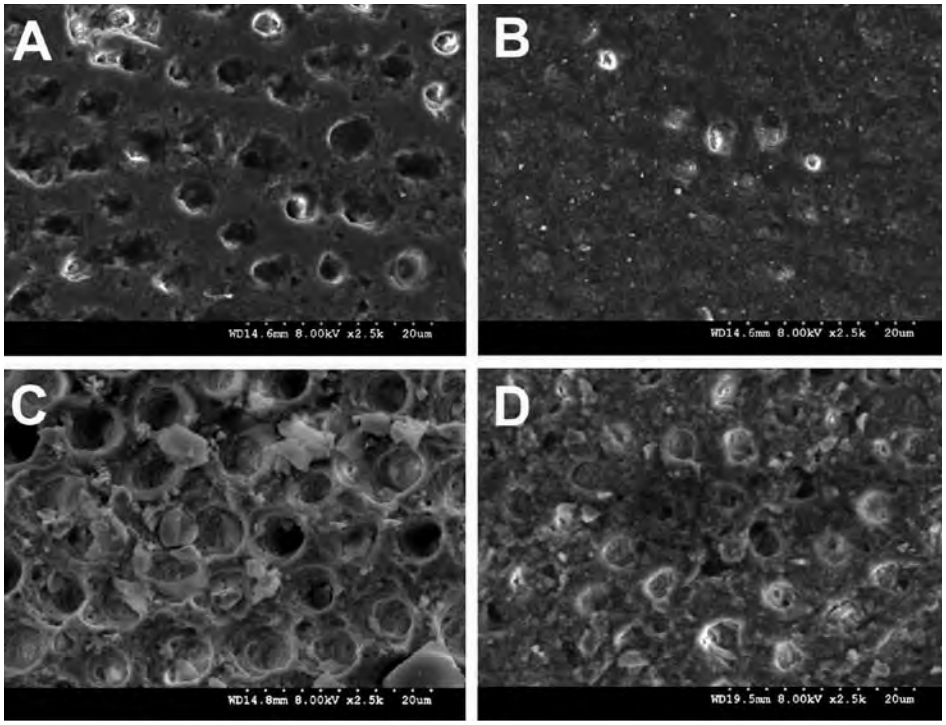


Fig. 4. 2500X SEM higher magnification micrographs of the dentine surface after air-polishing prophylactic procedures using prophy powders and pastes. The pictures **A** shows the effects of EMS Perio powder on the dentine surface. It is possible to observe that the dentinal tubules are completely or partially open. The pictures **B** shows the effect Sylc bioactive glass applied with the dental rubber cup induced the complete occlusion of the dentinal tubules leaving a dentine surface relatively smooth. The pictures **C** shows how Nupro NovaMin-containing paste created residual debris on the dentine surface. This debris are present also inside the tubules partially or completely occluding them. **(D)** The Sensitive Pro-Relief paste reduced the diameter and the number of the dentinal tubules. Many tubules can be seen completely occluded.

Table 2. Dentine permeability of the tested products.

Product	Max P% ($\mu Lmin^{-1}cm^{-2}$ cm H_2O^{-1})	Treatment P% ($\mu Lmin^{-1}cm^{-2}$ cm H_2O^{-1})	Permeability Reduction (P-R%)
Sylc bioactive glass® Powder	100%[1] (0.053)	11.2% [a2] (0.005)	88.8
Sylc bioactive glass H_2O	100%[1] (0.028)	17.1% [b2] (0.006)	81.1
Cavitron® *Prophy-Jet® sodium bicarbonate*	100%[1] (0.052)	19.7% [ab2] (0.018)	80.3
AIR-flow® powder PERIO	100%[1] (0.054)	31.2% [c2] (0.017)	68.8
Colgate® Sensitive Pro-Relief™	100%[1] (0.029)	30.2%[c2] (0.008)	69.8
NUPRO® NUSolutions™ Prophy Paste.	100%[1] (0.028)	33.1%[c2] (0.009)	66.9

The values of dentine permeability (Lp) are reported as percentage (P%) and $\mu Lmin^{-1}cm^{-2}$ cm H_2O^{-1}. Lp after 37% H_3PO_4 treatment was considered the maximum permeability (Lp = 100%). Same letter indicates no differences in columns with different products of the percentage of dentine permeability reduction –Lp%. Same number indicates no differences in row between PA-etched and products treated-dentine permeability.

Discussion

The general acceptance of the concept of the hydrodynamic theory postulated by Brännström *et al*, (8) has resulted in clinical research that it is possible to reduce dentine hypersensitivity by two different approaches: (i) Reduce the ability of the intradental nerves to respond to stimulations (7, 9, 21, 22) (ii) Reduce stimuli-evoked fluid shifts in the dentinal tubules by reducing dentine permeability (10, 23, 24).

However, the approach to reduce dentine hypersensitivity by enhancing the functional occlusion of dentinal tubules is the only method to achieve the decrease the dentine permeability (19, 24-27).

Several desensitizing agents have been employed to accomplish the reduction of the dentine permeability (10, 18, 25, 26, 28, 29). However, little information is available on the effects of prophylactic treatments on dentine permeability. Prophylaxis pastes are commonly used in dentistry to remove dental biofilm and stains. During the PRC prophylaxis process, as well as during air polishing procedures with different prophy-powders, dentine hypersensitivity may increase (18).

Air-polishing has been used for twenty five years for professional tooth cleaning as an alternative to pastes and rubber instruments (30, 31). The aim of the air-polishing procedures is the removal of the plaque and of extrinsic discolorations. The prophy-powder commonly used with air-polishing systems is sodium bicarbonate ($NaHCO_3$) with particle dimensions in the range of 100 - 200 μm (14, 15).

Recently, an amino-acid-glycine powder has been thought to be of help in periodontal treatment as well as for air-polishing (17, 32, 33). Whereas, "bioactive glass" prophy-powder constituted by calcium sodium phosphosilicate has been proposed for therapeutic and bioactive air-polishing procedures due to its capacity to react with saliva and deposit hydroxycarbonate apatite (HCA) (34, 35). The results of this study demonstrated that Sylc bioactive glass and Prophy-Jet sodium bicarbonate powders were the most effective in reducing the dentine permeability of PA-etched middle dentine at 4 bar of pressure (Table 1).

However, air-polishing procedures performed using Sylc bioactive glass (P% 11.2%) showed statistically higher permeability reduction compared to Prophy-Jet sodium bicarbonate (P% 19.7%) used at 4 bar of pressure in middle dentine. Sauro *et al*, (18) have recently shown that when these two air-polishing powders were used at higher pressure (i.e. 5 bar), no statistical difference, in terms of dentine permeability reduction, could be observed between the two materials. The SEM analysis suggests that this difference may be attributed to the lower pressure parameters used in this study which were probably insufficient for the sodium bicarbonate to create a compact smear layer on the exposed dentine.

Lower dentine permeability reduction was observed in the group of air-polished specimens with EMS Perio powder (-68.8). These results may be due to the absence of a consistent smear layer deposited on the surface but only to the presence dentinal tubules completely or partially open (Fig 2.D, 4.A). On the contrary, the use of Sylc bioactive glass and Prophy-Jet sodium bicarbonate formed a smear layer (Fig. 2.B, 2.C) that covered the exposed PA-treated dentine (Fig. 2.A).

Recent studies have shown that glycine-based powders have lower abrasiveness compared to other bicarbonate-based prophy-powders (32, 36). Indeed, this type of softer prophy-powder has been developed to be safely applied subgingivally during supra- and subgingival deplaquing (17). Nevertheless, the efficacy of glycine-based powders as dentine desensitizing seems to be inferior to that of the bioactive glass and sodium bicarbonate powders. Although the dentine permeability results of this study have been obtained in middle dentine and with a lower delivering pressure (i.e. 4 bar), they offer a wider view on the desensitizing capability of these prophylactic products when correlated to those of Sauro *et al*, (18) who tested the same materials tested on deep dentine at 5 bar of pressure. It is now possible to affirm that higher delivering pressure is an important parameter to consider when using sodium bicarbonate, but not when using Sylc bioactive glass. On the contrary, the different number of tubules and the reduced tubular fluid flow seem to be factors not primarily important to the performance of the prophy powders in reducing the dentine permeability.

The results are supported by the SEM investigation which showed that Sylc bioactive glass and Prophy-Jet sodium bicarbonate were able to create a consistent smear layer after their application on exposed dentine (Fig. 2.B) whereas, the air polishing performed with ESM Perio powder created a thin smear layer on the dentine surface and only some powder/smear plugs inside the tubule (Fig. 4.A).

It has been recently demonstrated that non-surgical treatments of scaling and root-planing performed using hand curette were able to create a more compact and multilayered acid resistant smear layer than that using an ultrasonic device which created a thin smear layer on the root dentine surface (5). The authors speculate on the concept of "resistance of the smear layer morphology" which is based on the fact that a highly porous smear layer is less effective to keep dentinal tubules occluded under acid challenge (5). Our hypothesis is that the application Sylc bioactive glass creates a smear layer much more compact and a bioactive intimate contact with the exposed dentine. Moreover, the bioactive characteristics of this material and the compact smear layer created during prophylactic procedures might offer the possibility of HA-deposition (remineralization) when exposed to fluids containing calcium and phosphate, such as saliva and tubular fluid (35).

Different results were observed when the specimens were treated with the prophy-pastes applied using PRC. Although most of the prophy-pastes used in this study were able to statistically reduce the dentine permeability of PA-etched dentine specimens, no more than 70%, of dentine permeability reduction was obtained. It is important to consider that several *in vivo* (19, 28; 36) and *in vitro* (20, 38-41) studies consider a gold standard treatment for dentine hypersensitivity the use oxalates which decrease dentine permeability by about 90% by creating acid-resistant calcium oxalate crystals both on the dentine surface and inside dentinal tubules.

The prophy-pastes applied with the PRC resulted in less dentine permeability reduction and in the reduced capacity to occlude the dentinal tubules compared to those of air-polished specimens (i.e. Sylc bioactive glass, Prophy-Jet sodium bicarbonate) also when applied in middle dentine. However, when Sylc bioactive glass was applied using a dental rubber cup it was possible to obtain a statistically higher dentine permeability reduction (-81.8%) compared to the other prophy-pastes used in this study. Thus, this may be an interesting alternative, in terms of dentine permeability reduction, to the current prophy-pastes.

The specimens treated with Colgate Sensitive Pro-Relief and NUPRO Solution Prophy-paste showed dentine permeability reduction of -69.8% and -66.9% respectively; no statistical difference was observed between these two commercial prophy-pastes. The SEM investigation showed that when Colgate Sensitive Pro-Relief was applied on exposed dentinal tubules only partial occlusion of the tubules was achieved. The most important observation in these specimens was the reduction of the lumen of the dentinal tubules. These results are in contrast with those of Petrou *et al*, (42) who reported recently that the application of Colgate Sensitive Pro-Relief was able to completely occlude the dentinal tubules. The differences may be attributed to the fact that in our study this prophy-paste was applied only once for 30s, while the authors of that paper obtained the maxi-

mum occlusion of the tubule and of the highest dentine permeability reduction after higher number of treatments (5 applications). The same observation may be applied to the use of NUPRO® NUSolutions™, a Prophy Paste containing NovaMin® indicated for the immediate treatment of dentine hypersensitivity. Indeed, although NovaMin® is a calcium sodium phosphosilicate bioactive glass with osteoinductive properties and forms carbonate hydroxyapatite when used in oral health care, our SEM investigation showed that the application of this product only superficially covered the exposed dentine surface with residual debris. This debris was found inside the dentinal tubules which only partially occluding them.

In conclusion, prophylactic procedures performed in middle dentine at lower working pressure are able to statistically reduce the dentine permeability and occlude the dentinal tubules. However, in situations of different morphological and pressure working parameters, the use of Sylc bioactive glass proved to be a suitable prophy-powder for dental air-polishing able to completely occlude the exposed dentinal tubules and reduce the dentine permeability.

References

1. von Troil B, Needleman I, Sanz M. A systematic review of the prevalence of root sensitivity following periodontal therapy. J Clin Periodont 2002; 29: 173-77.
2. Crespi R, Barone A, Covani U. Histologic evaluation of three methods of periodontal root surface treatment in humans. J Periodontol. 2005; 76:476-71.
3. Fiocchi MF, Moretti AJ, Powers JM, Rives T. Treatment of root sensitivity after periodontal therapy.Am J Dent. 2007; 20:217-20.
4. Kawashima H, Sato S, Kishida M, Ito K. A comparison of root surface instrumentation using two piezoelectric ultrasonic scalers and a hand scaler in vivo. J Periodontal Res. 2007; 42: 90-5.
5. Sauro S, Mannocci F, Watson TF, Piemontese M, Sherriff M, Mongiorgi R. The influence of soft acidic drinks in exposing dentinal tubules after non-surgical periodontal treatment: a SEM investigation on the protective effects of oxalate-containing phytocomplex. Med Oral Patol Oral Cir Bucal 2007; 12: E542-48.
6. Pashley DH, Mattews WG, Zhang Y, Johnson M. Fluid shifts across human dentin in vitro in response to hydrodynamic stimuli. Arch Oral Biol 1996; 41: 1065–72.
7. Addy M. Tooth brushing, tooth wear and dentine hypersensitivity--are they associated? Int Dent J. 2005; 55: 261-67.
8. Brännström M, Linden LA, Johnson G. Movement of dentinal and pulpal fluid caused by clinical procedures. J Dent Res 1968; 47: 679–82.
9. Addy M, Dowell P. Dentine hypersensitivity--a review. Clinical and in vitro evaluation of treatment agents. J Clin Periodontol 1983; 10: 351-63.
10. Pashley DH. Dentin permeability, dentin sensitivity and treatment through tubule occlusion. J Endod 1986; 12: 465–74.
11. Pashley DH. Dentin permeability and dentin sensitivity. Proc Finn Dent Soc. 1992; 88:31-7.
12. Jost-Brinkmann PG. The influence of air polishers on tooth enamel. An in-vitro study. J Orofac Orthop 1998; 59: 1-16.
13. Pikdoken ML, Ozcelik C. Severe enamel abrasion due to misuse of an air polishing device. Int J Dent Hyg. 2006; 4: 209-12.
14. Banerjee A, Hajatdoost-Sani M, Farrell S, Thompson I. A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air-polishing powders. J Dent. 2010; 38: 475-79.
15. Tada K, Kakuta K, Ogura H, Sato S. Effect of particle diameter on air polishing of dentin surfaces. Odontology. 2010; 98: 31-6.
16. Jepsen S, Ayna M, Hedderich J, Eberhard J. Significant influence of scaler tip design on root substance loss resulting from ultrasonic scaling: a laserprofilometric in vitro study. J Clin Periodontol. 2004; 31: 1003-6.
17. Moëne R, Décaillet F, Andersen E, Mombelli A. Subgingival plaque removal using a new air-polishing device. J Periodontol. 2010; 81: 79-88.
18. Sauro S, Watson TF, Thompson I. Dentine desensitization induced by prophylactic and air-polishing procedures: an in vitro dentine permeability and confocal microscopy study. J Dent. 2010; 38:411-22.
19. Orchardson R, Gillam DG. The efficacy of potassium salts agents for treating dentin hypersensitivity. I Orofac Pain 2000; 14: 9-20.
20. Sauro S, Gandolfi MG, Prati C, Mongiorgi R. Oxalate-containing phytocomplexes as dentine desensitisers: an in vitro study. Arch Oral Biol. 2006; 51: 655-64
21. Gillam DG, Orchardson R. Advances in the treatment of root dentin sensitivity: mechanisms and treatment principles. Endodontic Topics 2006; 13: 13–33.
22. Noparatkailas S, Wanachantararak S, Vongsavan N, Matthews B. The effect of applying potassium chloride solutions at atmospheric pressure on the sensitivity of dentine in man. Arch Oral Biol. 2009; 54: 50-4.
23. Bekes K, Schmelz M, Schaller HG, Gernhardt CR. The influence of application of different desensitisers on root dentine demineralisation in situ. Int Dent J. 2009; 59: 121-26.
24. Hamlin D, Williams KP, Delgado E, Zhang YP, DeVizio W, Mateo LR. Clinical evaluation of the efficacy of a desensitizing paste containing 8% arginine and calcium carbonate for the in-office relief of dentin hypersensitivity associated with dental prophylaxis. Am J Dent. 2009; 22: 16-20.
25. Pashley DH, Tao L, Boyd L, King GE, Horner JA. Scanning electron microscopy of the substructure of smear layer in human dentine. Arch Oral Biol 1988; 33: 265-70.
26. Pashley DH. Mechanisms of dentin sensitivity. Dent Clin North Am 1990; 34: 449-73.
27. Rusin RP, Agee K, Suchko M, Pashley DH. Effect of a new desensitizing material on human dentin permeability. Dent Mater. 2010; 26: 600-7.
28. Muzzin KB, Johnson R. Effects of potassium oxalate on dentin hypersensitivity in vivo. J Periodontol 1989; 60: 151-8.
29. Wang Z, Sa Y, Sauro S, Chen H, Xing W, Ma X, Jiang T, Wang Y.Effect of desensitising toothpastes on dentinal tubule occlusion: a dentine permeability measurement and SEM in vitro study. J Dent. 2010;38: 400-10.
30. Willmann D, Norling B, Johnson W. A new prophylaxis instrument. Effect on enamel alterations. J Am Dent Assoc 1980; 101: 923-25.
31. Jost-Brinkmann PG. The influence of air polishers on tooth enamel. An in-vitro study. J Orofac Orthop. 1998;59:1-16.
32. Petersilka GJ, Steinmann D, Haberlein I, Heinecke A, Flemmig TF. Subgingival Plaque Removal in Buccal and Lingual Sites Using a Novel Low Abrasive Air polishing Powder. J Clin Periodontol 2003; 30: 328-33.
33. Petersilka G, Faggion Jr. CM, Stratmann U, Gerss J, Ehmke B, Haeberlein I, Flemmig TF. Effect of glycine powder air polishing on the gingiva. J Clin Periodontol 2008; 35: 324-32
34. Hench LL, Andersson Ö. Bioactive glasses. In: Introduction to bioceramics. Hench LL, Wilson J, editors. Singapore: World Scientific, 1993: 45-47.
35. Burwell AK, Litkowski LJ, Greenspan DC. Calcium Sodium Phosphosilicate (NovaMin®): Remineralization Potential. Adv Dent Res 2009; 21:35-39.
36. Kahl M, Haase E, Kocher T, Rühling A. Clinical effects after sub gingival polishing with a non-aggressive ultrasonic device in initial therapy. J Clin Periodontol 2007; 34: 318-24.

37. Zero DT, Lussi A. Etiology of enamel erosion: intrinsic and extrinsic factors. In: Addy M, Embery G, Edgar WM, Orchardson R, editors. Tooth wear and sensitivity. London: Martin-Dunitz; 2000; [chapter 11]: 121-39.
38. Kerns DG, Scheidt MJ, Pashley DH, Horner JA, Strong SL, Van Dyke TE. Dentinal tubules occlusion and root hypersensitivity. J Periodontol 1991; 62: 421-428.
39. Mongiorgi R, Tateo F, Monti S, Prati C, Bertocchi G. Calcium oxalate smear layer: mineralogical and crystallographic study. Boll Soc Ital Biol Sper. 1992;68:99-03.
40. Gillam DG, Mordan NJ, Sinodinou AD, Tang JY, Knowles JC, Gibson IR. The effects of oxalate-containing products on the exposed dentine surface: an SEM investigation. J Oral Rehabil 2001; 28: 1037-44.
41. Suge T, Kawasaki A, Ishikawa K, Matsuo T, Ebisu S. Ammonium hexafluorosilicate elicits calcium phosphate precipitation and shows continuous dentin tubule occlusion. Dent Mater 2008; 24: 192-198.
42. Petrou I, Heu R, Stranick M, Lavender S, Zaidel L, Cummins D, Sullivan RJ, Hsueh C, Gimzewski JK. A breakthrough therapy for dentin hypersensitivity: how dental products containing 8% arginine and calcium carbonate work to deliver effective relief of sensitive teeth. J Clin Dent 2009; 20: 23-31.

Acknowledgments
This study was supported by the Department of Health via the National Institute for Health Research (NIHR) comprehensive Biomedical Research Centre award to Guy's & St Thomas' NHS Foundation Trust in partnership with King's College London and King's College Hospital NHS Foundation Trust and OSspray Ltd. Company, London, UK.

©Operative Dentistry, 2011, **36-2,** 222-230

Effects of Common Dental Materials Used in Preventive or Operative Dentistry on Dentin Permeability and Remineralization

S Sauro • I Thompson • TF Watson

CLINICAL RELEVANCE

The bioactive glass (Sylc) reacts with saliva depositing hydroxycarbonate apatite (HCA) within the demineralized collagen fibrils and occluding dentinal tubules. Therefore, it may be used as a suitable desensitizing bioactive material for the treatment of DH and as an air-cutting powder before bonding procedures to remineralize tooth structure and/or prevent further demineralization within the resin–dentin interface.

SUMMARY

The aim of this study was to evaluate the dentin remineralization induced by bioactive substances contained in common dental materials used in preventive and operative dentistry. Several materials were applied on human dentin segments. Dentin permeability was quantified using a fluid filtration system working at 20 cm H_2O. Micro-Raman, SEM-EDX, and microhardness calculation were used to evaluate changes in the mineralization of dentin. Dentin treated with the prophylactic materials showed different dentin permeability values, in particular subsequent to immersion in remineralizing solutions (RSS). The bioactive glass (Sylc) was the only substance able to reduce dentin permeability after immersion in remineralizing solution and to show hydroxyapatite precipitation as a sign of dentin remineralization. The reduction in dentin permeability obtained after the application of the other prophylactic mate-

*Dr. Salvatore Sauro, PhD, associate researcher, Biomaterials, Biometrics & Biophotonics, King's College London Dental Institute, Guy's, King's College and St Thomas' Hospitals, London, United Kingdom

Dr. Ian Thompson, PhD, senior lecturer, Biomaterials, Biometrics & Biophotonics, King's College London Dental Institute, Guy's Hospital, London SE1 9RT, United Kingdom

Professor Timothy F Watson, BSc, BDS, PhD, FDS, professor and chairman, Biomaterials, Biometrics & Biophotonics, King's College London Dental Institute, Guy's, King's College and St Thomas' Hospitals, London, United Kingdom

*Corresponding Author: Floor 17, Guy's Tower, London, SE1 9RT, England

DOI: 10.2341/10-225-L

rials used in this study was due to the presence of the remnant material in the dentinal tubules, with no remineralization effect after storage in remineralizing solution. In conclusion, the results indicated that bioactive glass prophy powder may induce immediate remineralization of dentin.

INTRODUCTION

Dentin hypersensitivity (DH) is caused principally by the movement of the intratubular fluid after the exposure of dentin due to enamel loss and/or gingival root surface exposure.[1-3] The consumption of acidic food and beverages may cause erosion of hard dental tissues and increase the risk for DH.[4,5] Indeed, an essential association exists between the frequency of ingestion of specific acidic foods and beverages with the exposure of dentinal tubules.[6-8] Furthermore, the tooth brushing subsequent to the assumption of dietary acids may enhance the exposure of the dentinal tubules and aggravate the DH.[7,9]

Desensitizing bioactive materials involved in the treatment of DH should be able to react with body fluids and/or saliva depositing hydroxycarbonate apatite (HCA) within the demineralized collagen fibrils and occluding dentinal tubules.[10,11] Mineralizing processes may also occur via the tubular fluid, which is very similar to the extracellular fluid and, in conjunction with the odontoblast processes, orchestrates mineralization processes.[12-14]

The aim of this article is to present a series of experiments performed to test the ability of bioactive substance contained in prophy pastes or air polishing/cutting powders in encouraging the dentin remineralization and occlusion of the dentinal tubules. The null hypothesis tested in this study was that all prophy pastes or powders containing bioactive principles are capable of occluding dentinal tubules and remineralizing the dentin tissue when immersed in a remineralizing saline solution (RSS) for 24 or 48 hours.

MATERIALS AND METHODS

Dentin Permeability Evaluation

Thirty-five human third molars recently extracted for surgical reasons were used in this study. Dentin crown segments were obtained by first removing the roots 1.0 mm beneath the cementum-enamel junction (CEJ) using a slow-speed water-cooled diamond saw (Labcut; Agar Scientific, Stansted, UK). The occlusal enamel was subsequently removed with a parallel cut to expose the deep dentin. Pulpal tissue was carefully removed from the exposed pulp chamber by using tissue forceps. The remaining dentin thickness (RDT) was 0.7 and 0.9 mm. The specimens were divided in seven groups (n=5) in accordance with the materials listed in Table 1. The specimens were positioned in a modified Perspex™ (Perspex Distributions Ltd, London, UK) split-chamber device with pairs of rubber "O" rings with an internal diameter of 5 cm to standardize the dentin surface for fluid filtration.[15] A 25-μL-capacity microcapillary tube (Microcaps; Fisher Scientific, Atlanta, GA, USA) was horizontally positioned between the pressure reservoir (20 cm H_2O) and the dentin surface. The hydraulic conductance obtained via a microcapillary tube was converted into the dentin permeability (Lp): Lp=Q/At, where Lp is the dentin permeability ($\mu L\ cm^{-2}\ min^{-1}$), Q is the fluid flow (μL), A is the area of the dentin (cm^2), and t is the time (minutes).[16]

A homogeneous smear layer was created using a 500-grit abrasive paper for 30 seconds to evaluate the minimum dentin permeability. The smear layer was then removed, treating the dentin surface using 35% orthophosphoric acid solution (PA) for 30 seconds, and the highest permeability (Lp max=100% arbitrarily assigned) was evaluated. Lp 100% permits evaluation of modifications in dentin permeability following the test treatments. The specimens of each group were then treated with the experimental products in order to calculate the dentin permeability and expressed as a percentage (Lp%) of the maximum Lp value (100%). Since the intent of this study was the evaluation of the remineralization of dentin and of the capacity to occlude the dentinal tubules by mineral formation, the specimens were treated by spreading the products using gentle strokes and a camel hair brush. Finally, the samples were gently rinsed to ensure removal of any excess product and stored in RSS for 24 and 48 hours to evaluate the effect of the remineralization on the dentin permeability. The RSS solution (in g/L) was $CaCl_2$ (0.103), $MgCl_2 \cdot 6H_20$ (0.019), KH_2PO_4 (0.544), KCl (30), and HEPES (acid) buffer (4.77), and the pH was 7.4. The RSS solution was replaced every 12 hours. In this study a 0.3% solution of citric acid (pH 3.2) was also used for 5 minutes to test the ability of each test sample to resist an acidic attack.[15]

Raman Microscopy Evaluation

Thirty-five dentin specimens (2×2 mm) with thickness of 1.5±0.1 mm were totally demineralized in 0.02 M citric acid (pH 3.5) for 72 hours under constant stirring (120 rpm/s) at 37°C. The specimens were then copiously rinsed with deionized water and

Table 1: *Dentin Permeability and Microhardness of the Tested Products*

Active Ingredients	Max Lp% (Etched Dentin)	Immediate Application			PBS, 24 h
		Dentin Permeability, %[a]	Dentin Permeability Reduction, %[b]	Microhardness of Dentin Surface[c]	Dentin Permeability, %[a]
3 wt% monopotassium-monohydrogen oxalate in water NaH C_2O_4 H_2O pH 2.7	100	9.5 ± 1.4 ^{A1}	δ −91.5	89.1 ± 1.5 ^{a1}	9.6 ± 1.5 ^{A1}
Bioactive glass 100% SiO_2, Na_2O, CaO P_2O_5 SYLC (Osspray Ltd, London, UK)	100	99.6 ± 5.2 ^{B1}	δ −0.4	90 ± 1.3 ^{a1}	21.3 ± 6.2 ^{A2}
Sodium bicarbonate NaHCO3 Cavitron® Prophy Powder (Dentsply Corp, London, UK)	100	98.3 ± 3.5 ^{B1}	δ −1.7	89.2 ± 1.1^{a1}	98.5 ± 3.7 ^{B1}
Amino-acid-glycine NH_2CH_2COOH EMS Perio (EMS Corp,) Nyon, Switzerland)	100	98.9 ± 4.1 ^{B1}	δ −1.1	90.1 ± 1.2 ^{a1}	91.6 ± 4.5 ^{B1}
CPP-ACP: casein and phosphopeptide-amorphous calcium phosphate § GC Tooth Mousse (GC Corp, Tokyo, Japan)	100	59.8 ± 9.5 ^{C1}	δ −40.2	88.9 ± 0.8 ^{a1}	56.8 ± 9.1 ^{C1}
8% calcium carbonate-arginine § Colgate Sensitive Pro-Relief (Colgate Palmolive, New York, NY, USA)	100	80.4 ± 6.5 ^{B1}	δ −19.6	89.9 ± 0.9 ^{a1}	79.8 ± 6.4 ^{D1}
5% calcium sodium phosphosilicate NovaMin® § NUPRO Solution Prophy Paste (Dentsply)	100	85.6 ± 4.5 ^{B1}	δ −14.4	88.9 ± 1.1 ^{a1}	76.5 ± 4.6 ^{D1}

[a] Reported as means. Lp after 35% PA treatment was considered the maximum permeability (Lp=100%).
[b] −Lp% between treatments and Max permeability.
[c] Numbers in brackets represent the microhardness of the dentine surface [KHN].
Same uppercase letter indicates no differences in columns with different product treatments maintained in the same media. Same number indicates no differences in rows for time of RSS immersion (p>0.05).
The products with the symbol § contain other ingredients mixed with the active principle. GC Tooth Mousse™: glycerol, D-sorbitol, silicon dioxide, CMC-Na, propylene glycol, titanium dioxide, xylitol, phosphoric acid, zinc oxide, sodium saccharin, ethyl p-hydroxybenzoate, magnesium oxide, butyl p-hydroxybenzoate, and propyl p-hydroxybenzoate; Sensitive Pro-Relief™: hydrated silica, glycerin, water, bicarbonate, flavor, cellulose gum, sodium saccharin; NUSolutions™: hydrated silica, glycerin, water, bicarbonate, flavor, cellulose gum, sodium saccharin.

treated with the experimental products as described above. Control specimens were stored in deionized water, while the dentin specimens treated with different products were immersed in the RSS solution for 24 and 48 hours.

Subsequent to the remineralization periods, the specimens were examined in wet condition using a computer-controlled confocal laser Raman apparatus equipped with a Leica DM/LM optical microscope with a 20× objective and CCD detector attached to a modular research spectrograph (Renishaw InVia; Renishaw plc, Gloucheshire, UK). A near-infrared diode laser spot size of ≤1 μm operating at 785 nm was used to induce the Raman scattering effect. The spectral coverage of this model ranges from 200 to 3000 cm^{-1}. The calibration of the wavelength and intensity was performed according to manufacturer's specification using a silicon standard and the calibration system integrated with the software (WiRE 3.2; Renishaw) . The entire dentin surfaces were examined with steps of 10.0 ìm on the X and Y axes using a computer-motorized stage and analyzed for the peak of hydroxyapatite at 961 cm^{-1} using the software Wire 3.2 (Renishaw).[20,21]

SEM-EDX Evaluation

Following the nondestructive procedure of Confocal Raman characterization, the specimens were im-

Table 1: *Dentin Permeability and Microhardness of the Tested Products (ext.)*

PBS, 24 h		PBS, 48 h			Citric Acid		
Dentin Permeability Reduction, %[b]	Microhardness of Dentin Surface[c]	Dentin Permeability, %[a]	Dentin Permeability Reduction, %[b]	Microhardness of Dentin Surface[c]	Dentin Permeability, %[a]	Dentin Permeability Reduction, %[b]	Microhardness of Dentin Surface[c]
δ −91.4	89.5 ± 1.4 [a1]	9.6 ± 1.6 [A1]	δ −91.4	89.5 ± 1.4 [a1]	9.8 ± 1.1[A1]	δ −91.2	89.8 ± 2.1 [a1]
δ −78.7	60.1 ± 3.5 [b2]	20.9 ± 5.9 [A2]	δ −79.1	57 ± 3.4 [b2]	38.9 ± 5.5 [B2]	δ −61.1	85.3 ± 1.3 [a1]
δ −1.5	86.7 ± 1.0 [a1]	97.3 ± 3.5 [B1]	δ −2.7	86.1 ± 0.9 [a1]	106.8 ± 6.5 [C1]	δ +6.8	89.1 ± 1.2 [a]
δ −8.4	88.9 ± 1.1 [a1]	93.4 ± 5.1 [B1]	δ −6.6	88.6 ± 1.1 [a1]	105.2 ± 5.5 [C1]	δ +5.2	89.9 ± 0.9 [a1]
δ −43.2	80.2 ± 1.1 [a1]	54.3 ± 8.5 [C1]	δ −45.7	78.9 ± 1.1 [a1]	84.2 ± 9.1 [D2]	δ −15.8	89.5 ± 1.0 [a1]
δ −20.2	88.1 ± 1.0 [a1]	79.1 ± 6.3 [D1]	δ −20.9	87.7 ± 1.1 [a1]	89.7 ± 5.5 [D1]	δ −10.3	89.1 ± 0.8 [a1]
δ −23.5	87.1 ± 0.9 [a1]	74.9 ± 4.5 [D1]	δ −25.1	87.7 ± 1.0 [a1]	85.1 ± 5.1 [D1]	δ −4.9	89.3 ± 1.0 [a1]

mersed in deionized water for 1 hour and then dehydrated, mounted on aluminum stubs, and sputter-coated with carbon. The morphology and microstructure of the specimens were analyzed using a Hitachi S3500 scanning electron microscope (Hitachi High Technologies, Maidenhead, UK) fitted with an Oxford Instruments Inca energy dispersive X-ray microanalysis system (EDX) (Oxford Instruments, Abingdon, UK) under conditions of 8 kV of accelerating voltage.

Microhardness Evaluation

Another thirty-five dentin discs (2×2 mm) with thickness of 1.5±0.1 were partially demineralized by immersion in a citric acid solution (0.02 M; pH 3.5) for 5 minutes. Microhardness, in terms of the Knoop hardness number (KHN), was performed using a Knoop indenter in a microhardness tester (Leitz Microhardness Tester; Ernst Leitz Wetzlar GmbH, Wetzlar, Germany) with a load of 100 g with a dwell time of 20 seconds. Each dentin slice was considered as a sample unit. Five measurements were randomly obtained in wet condition from each dentin surface and elaborated using the formula of the Method for Knoop Indentation Hardness of Advanced Ceramics (KHN=constant×test force/indent diagonal squared). The dimensions of all indentations were measured immediately following indentation to avoid possible shrinkage caused by mechanical recovery of the tooth surfaces.

Statistical Analysis

Statistical analysis was performed using the SPSS 16.0 (SPSS Inc., Chicago, IL, USA) program. Shapiro-Wilk W-test and the Levene test were used for the validation and normality of the results. Statistical differences were identified by two-way analysis of variance evaluating the effect of different prophylactic measures and the different challenges differences ($p<0.01$). Fisher's least significant difference test was used to isolate and compare the significant differences ($p<0.05$) between the groups.

RESULTS

Dentin Permeability Evaluation

The permeability of the PA etched-dentin specimens was arbitrary considered equal to 100% and represented the own control of each specimen subsequently treated with one of the experimental treatments.

All the products used in this study differently influenced the dentin permeability both immediately after the application and after RSS immersion (Table 1). For instance, 3 wt% monopotassium-monohydrogen oxalate induced the highest dentin permeability reduction (−91.5%). Subsequent to immersion in RSS and in citric acid, no statistical change was observed.

The bioactive glass, sodium bicarbonate, and amino-acid glycine powders applied on acid-etched dentin induced no statistical reduction in dentin permeability immediately subsequent to the application. Conversely, when the bioactive glass (Sylc) was applied on the demineralized dentin and subsequently immersed in RSS for 24 hours, a statistical reduction in dentin permeability was observed; the reduction of the dentin permeability after 48 hours of RSS immersion was −79.1%. Sodium bicarbonate (Cavitron Prophy Powder) and amino-acid glycine (EMS Perio) prophy powders showed no dentin permeability reduction after RSS immersion, and the citric acid attack increased the dentin permeability more than their own control (Table 1).

Regarding the application of the prophy paste containing casein/phosphopeptide-amorphous calcium phosphate (GC Tooth Mousse), a permeability reduction up to −40.2% was observed after the application, while the prophy paste containing 8% calcium carbonate-arginine (Colgate Sensitive Pro-Relief) and the prophy paste containing 5% calcium sodium phosphosilicate (NovaMin®; NUPRO Solution) showed a permeability reduction of −19.6% and −14.4%, respectively. However, these materials showed no further permeability reduction after RSS immersion; the citric acid attack increased the permeability of the treated dentin (Table 1).

Raman Microscopy Evaluation

The Raman spectroscopy showed that the sound dentin (control) was characterized by peaks spanning from 400 to 1100 cm^{-1} with the most prominent peaks at 961 cm^{-1}, which is representative of the mineral phase of the dentin ($\upsilon 1\text{-}PO_4^{3-}$; hydroxycarbonate apatite [HCA]).[17,18] Organic grouping vibration modes (amide and CH) representing the dentin collagen were detected in the 1200–3000-cm^{-1} region (Figure 1A-a). Conversely, totally demineralized dentin specimens showed no peaks in the region from 400 to 1100 cm^{-1}, indicating the absence of any phosphate group (Figure 1A-b) and a strong autofluorescence signal representing the organic components. The demineralized specimens treated with the bioactive glass (Sylc) and subsequently immersed in RSS showed peaks in the region from 400 to 1100 cm^{-1} with a prominent peak at 961 cm^{-1} (Figure 1A-c). The peak of HCA was not observed after application of sodium bicarbonate (Cavitron Prophy Powder) and RSS immersion, but, on the contrary, a strong signal representing the demineralized dentin collagen was clearly visible (Figure 1A-d). No HCA formation was detected during the Raman scanning both when the totally demineralized dentin specimens were treated with the other products and following the immersion in RSS for 24 and 48 hours (Figure 2B–E).

SEM-EDX Evaluation

The remineralization process with occlusion of the dentinal tubules were further investigated by scanning electron microscopy using an element-sensitive detector (EDX) to qualitatively record the element composition (Ca and P/O) within the dentin surface treated in accordance with the experimental design.[19] The control Ca and P/O ratios were recorded from the smear layer–covered dentin (Figure 2A). High Ca and P/O ratios were observed in this group of specimens (Figure 2a). Similar Ca/P and O ratios (Figure 2b) were detected from the specimens treated with the bioactive glass (Sylc) and immersed in RSS for 24 and 48 hours (Figure 2B). The application of sodium bicarbonate (Cavitron Prophy Powder) or amino-acid glycine (EMS Perio) with subsequent immersion in RSS did not induce any increase in the concentration of the Ca and P/O ratios of the dentinal tubules (Figure 2C,D).

Similar results were observed in the specimens treated with the prophy pastes; no particular increase in Ca and P/O ratios were detected from the tubules of these dentin specimens (Figure 3); a constant presence of silicon (Si) was instead observed (Figure 3c,d).

Microhardness Evaluation

The results of this experiment showed that the higher the value obtained by Knoop indentation hardness (KHN), the lower the superficial hardness of the dentin surface (Table 1). For instance, sound dentin (control) showed the highest superficial microhardness value (49.1). Conversely, dentin specimens totally demineralized showed a superficial microhardness value of 89.9 due to the visco-

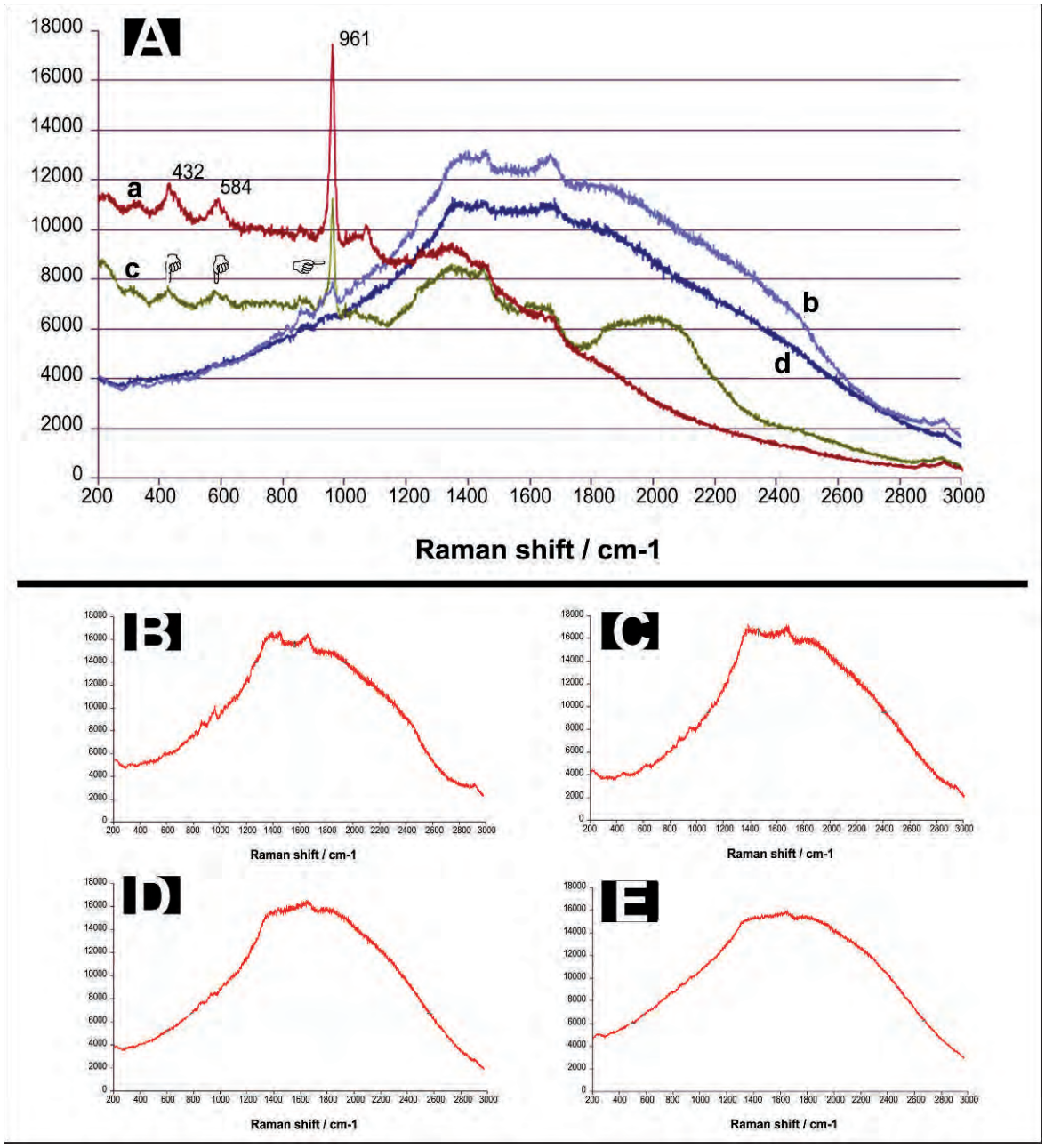


Figure 1. *Micro-Raman spectrums of dentin treated with the different remineralizing products and subsequently immersed in RSS for 24 and 48 hours. (A-a): Sound dentin is indicated by the presence of peaks at 432, at 584 cm^{-1}, and a peak with the highest intensity at 960 cm^{-1} representing the HCA component (pointers). (A-b): Totally demineralized dentin showing a Raman region spanning from 1200 to 3000 cm^{-1} representing the organic components of the dentin. (A-c): Raman spectra of the dentin treated with bioactive glass and immersed in RSS solution indicating the presence of peaks at 432, 584 cm^{-1}, and the highest peak at 960 cm^{-1} representing the formation and deposition of HCA. (A-d): Raman spectra of the dentin treated with CPP-ACP and immersed in RSS. It is possible to observe the presence of no peak for the HCA but only a high intensity region spanning from 1200 to 3000 cm^{-1} representing the organic components; the intensity of this region is slightly lower than that observed in the totally demineralized dentine (A-b). The same situation was observed in the specimens treated with sodium bicarbonate (B), arginine calcium-carbonate (C), Nupro containing 5% Novamin bioactive glass (D), and 100% amino-acid glycine (E).*

elastic characteristics of the demineralized dentin. Immediate application of the experimental products on the demineralized dentin showed no change in microhardness when compared to those obtained in the demineralized dentin specimens. Contrariwise, the immersion in RSS induced an increase of the superficial dentin microhardness only in those specimens treated with the bioactive glass (Sylc). No changes were observed in the specimens treated with the other products.

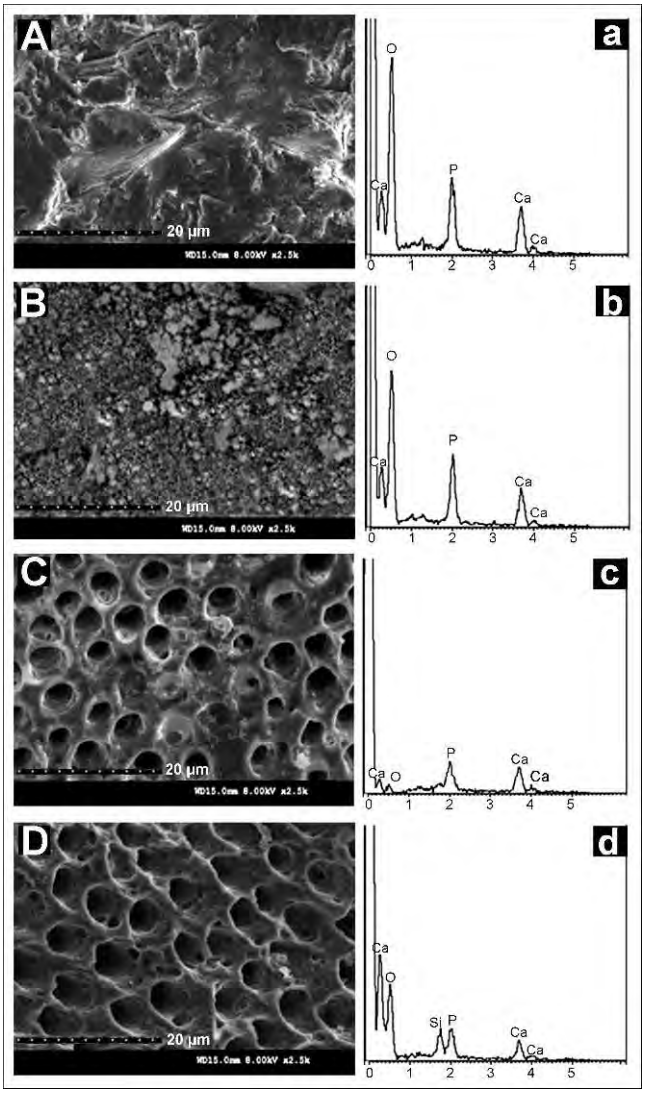


Figure 2. *SEM-EDX images of the smear layer–covered dentin (control), which shows no exposed dentinal tubule (A) and EDX spectra with high peaks of Ca and P/O characteristic of the mineralized dentin (a). The treatment of the demineralized dentin surface with bioactive glass (Sylc) and the immersion in RSS induced the precipitation of HCA (B). The EDX spectra of these specimens show presence of high Ca and P/O peaks comparable to those observed in the control specimens (b). The application of (Cavitron Prophy Powder) (C) or (EMS Perio) (D) induce no reliable HCA precipitation subsequent to RSS immersion (c, d).*

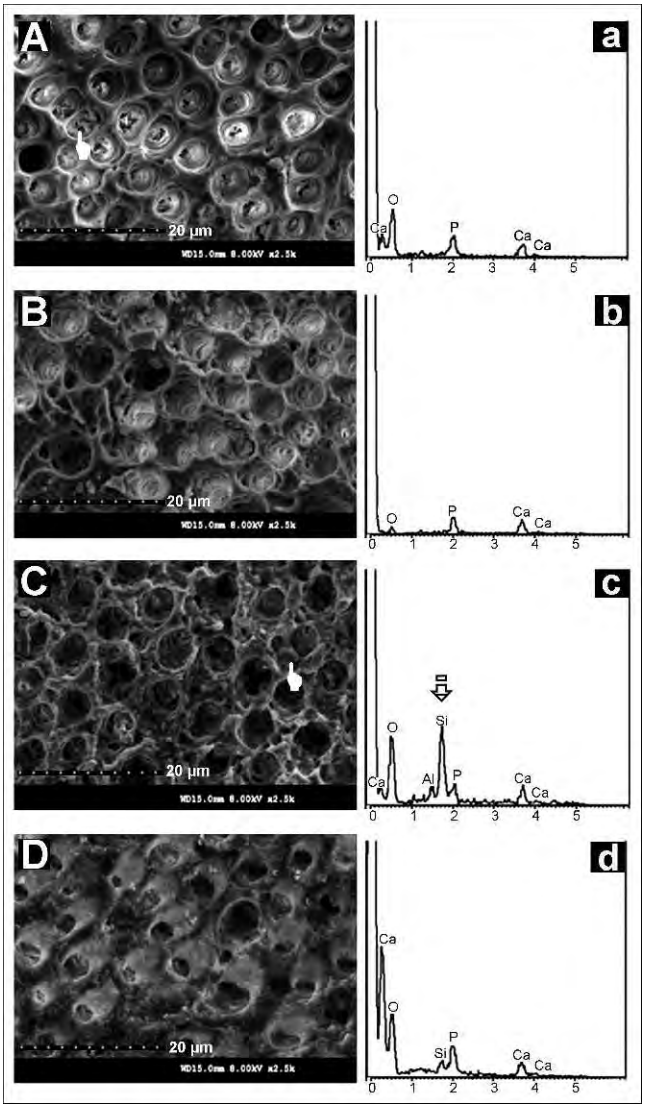


Figure 3. *(A): SEM-EDX micrographs of the dentin specimens treated with oxalic acid and immersed in RSS for 48 hours showing the presence of crystal-like deposits several microns deep inside the dentinal tubules (pointer). The EDX spectra shows low peaks of Ca and P/O on the dentin surface (a). The treatment of the demineralized dentin with Nupro NU Solutions™ and immersed in RSS induced no precipitation of HCA (B); the EDX spectra shows low peaks of Ca and P/O (a). (C): SEM-EDX micrograph of the dentin specimens treated with Colgate Sensitive Pro-Relief containing 8% arginine-calcium-carbonate and immersed in RSS for 48 hours showing the presence of many open dentinal tubules with very few debris on the dentin surface (pointer). Also in this case, the EDX spectra have low peaks of Ca and P/O (a) and a high presence of silicon (arrow) inside the dentinal tubules. The application of GC Tooth Mousse (D) induced no reliable HCA precipitation inside the tubules subsequent to RSS immersion but only a reduction of the lumen of the dentinal tubules (2–3 µm). Similarly, low peaks of Ca and P/O may be seen in this case (d) with the presence of silicon inside the dentinal tubules.*

DISCUSSION

The remineralization of dentin and the formation of crystalline apatite inside the dentinal tubules may be a reliable approach for the reduction of the dentin permeability in the clinical treatment of hypersensitivity.[11,12] Moreover, this concept may be considered for the reduction of the micropermeability within the hybrid layer of resin bonded dentin.[13] Many dental products used in preventive and operative dentistry have had manufacturer's claims that they can reduce the clinical symptoms of DH and induce dentin remineralization. Nevertheless, most of these materials are able to occlude the

dentinal tubule only via mechanical procedures that facilitate the formation of an artificial smear layer and smear plugs inside the tubules.[9,16] There is little information on the effective remineralizing potential of active components within the current clinical materials available.

The aim of this study was to perform a series of experiments to test the ability of bioactive substance contained in prophy pastes or air polishing/cutting powders in encouraging the remineralization and occlusion of the dentinal tubules. The experiments performed in this study have shown a significant dentin remineralization affect induced by the bioactive glass powder (Sylc) when compared to all the alternate test materials. Bioactive glasses encompass a wide range of clinical applications, some currently used as bone substitutes in periodontology, as load-bearing ceramic vertebral spacer prostheses, and as dentin desensitizing agents when used for air polishing procedures.[15,17] Bioactive glasses may also be used during restorative procedures in air-cutting/abrasion units as a substitute to alumina for an alternative nonmechanical cavity preparation. Its clinical use has many advantages, including reduced pain experienced by patients and selective removal of carious dentin and rounded internal cavity angle preparations that minimize stress concentration.[18]

The Raman microscopy evaluation showed that the demineralized dentin treated with Sylc bioactive glass and subsequently immersed in RSS for 24 and 48 hours was characterized by the reappearance of the peaks at 432, at 584 cm^{-1}, and a high intensity signal at 961 cm^{-1} (Figure 1Ac), indicating dentin remineralization.[19,20] The dentin remineralization observed in these specimens was confirmed by the microhardness results, which showed an increase in the superficial microhardness in demineralized Sylc bioglass-treated specimens immersed in RSS (Table 1). These results were not observed in any other group of specimens treated with the powders or prophy pastes used in this study. Indeed, there were no remineralization signals observed from any test material other than bioactive glass. The dentin spectra were comparable to those observed in totally demineralized dentin specimens, which showed a high intensity region spanning from 1200 to 3000 cm^{-1} (Figure 1Ab) representing the presence of demineralized dentin.[20]

The confirmation that the Sylc bioactive glass used in this study may be a suitable approach for the remineralization of dentin was also obtained by the evaluation of the dentin permeability. Indeed, the reduction of the dentin permeability was obtained only when exposed dentin was treated with Sylc bioactive glass powder and immersed in RSS for 48 and 48 hours (Table 1). Contrariwise, although the prophy pastes reduced the dentin permeability immediately after the application on demineralized dentin, no further reduction was observed after RSS immersion.

SEM-EDX investigation showed a spectrum with low peaks of Ca and P/O and a constant presence of silicon peaks inside the dentinal tubules (Figure 3). These results demonstrate that the reduction in dentin permeability observed in the specimens treated with the prophy pastes used in this study was induced by the occlusion of the tubules by the penetration of material plugs and not via HCA precipitation.[21] Conversely, SEM-EDX showed that the Sylc bioactive glass triggered the precipitation of HCA into the tubules and on the dentin surface (Figure 2B-b). The remineralization process induced by the Sylc bioactive glasses was due to a simultaneous biomimetic process, characterized by silicic acid $Si(OH)_4$ release, and a subsequent polycondensation reaction induced by precipitation of calcium and phosphates. Indeed, when calcium sodium phosphosilicate is immersed in a fluid analogous to saliva or body fluids, sodium ions (Na^+) immediately begin to exchange with hydrogen cations (H^+ or H_3O^+) within one minute.[22–24] This rapid exchange of ions allows calcium (Ca^{2+}) and phosphate (PO_4^{3-}) species to be released from the particle structure. A modest localized, transient increase in pH occurs and facilitates the precipitation of calcium and phosphate from the particles and from saliva to form an amorphous calcium phosphate layer ($CaO\text{-}P_2O_5$) on tooth surfaces and within the demineralized dentin. As the reactions and the deposition of Ca-P complexes continue, this layer crystallizes into hydroxycarbonate apatite, which is chemically and structurally similar to biological apatite.[22,23] The combination of the residual calcium sodium phosphosilicate particles and the HCA layer results in remineralization and physical occlusion of dentinal tubules. The chemical reactions initiated by calcium sodium phosphosilicate to promote the formation of an HCA might also be useful in treating demineralized tooth structure, preventing further demineralization and remineralizing the hybrid layer within the resin–dentin interface when used during bonding procedures. However, although Nupro NU Solutions™ is the only prophy paste containing bioactive glass doped with calcium and phosphate ions, this study has demonstrated that a single application and 24 or 48 hours of immersion in RSS solution is not sufficient for this product to induce dentin remineralization.

In conclusion, we have to reject the null hypothesis that all the dental materials used in this study are able to remineralize the dentin and occlude the dentinal tubules after immersion in a remineralizing saline solution (RSS) for 24 or 48 hours.

Further studies are in progress to evaluate the remineralization effects of the bioactive glass on the hybrid layers when used during air-cutting or bonding procedures to increase the longevity of the restorations.

ACKNOWLEDGMENT

This study was supported by the 2010 Ralph Phillips Research Fund of the Academy of Operative Dentistry. The authors also acknowledge support from the Department of Health via the National Institute for Health Research (NIHR) Invention for Innovation (i4i) Programme award to King's College London' Trust.

(Accepted 6 December 2010)

REFERENCES

1. Brännström M, Linden LA, & Johnson G (1968) Movement of dentinal and pulpal fluid caused by clinical procedures *Journal of Dental Research* **47(5)** 679-682.
2. Addy M & Pearce N (1994) Aetiological, predisposing and environmental factors in dentine hypersensitivity *Archives of Oral Biology* **39(Supplement)** 33S-38S.
3. Pashley DH, Mattews WG, Zhang Y, & Johnson M (1996) Fluid shifts across human dentin in vitro in response to hydrodynamic stimuli *Archives of Oral Biology* **41(11)** 1065-1072.
4. Addy M, Absi EG, & Adams D (1987) Dentine hypersensitivity: The effects in vitro of acids and dietary substances on root-planed and burred dentine *Journal of Clinical Periodontology* **14(5)** 274-279.
5. Lussi A, Kohler N, Zero D, Schaffner M, & Megert B (2000) A comparison of the erosive potential of different beverages in primary and permanent teeth using an in vitro model *European Journal of Oral Science* **108(2)** 110-114.
6. Clark C, Woo G, Silver JG, Sweet D, & Grisdale JC (1990) The influence of frequent ingestion of acids in the diet on treatment for dentin sensitivity *Journal of the Canadian Dental Association* **56(12)** 1101-1103.
7. Absi EG, Addy M, & Adams D (1992) Dentine hypersensitivity—The effect of toothbrushing and dietary compounds on dentine in vitro: A SEM study *Journal of Oral Rehabilitation* **19(2)** 101-110.
8. West NX, Hughes JA, & Addy M (2001) The effect of pH on the erosion of dentine and enamel by dietary acids in vitro *Journal of Oral Rehabilitation* **28(9)** 860-864.
9. Prati C, Montebugnoli L, Suppa P, Valdre G, & Mongiorgi R (2003) Permeability and morphology of dentin after erosion induced by acidic drinks *Journal of Periodontology* **74(4)** 428-436.
10. Litkowski LJ, Hack GD, Sheaffer HB, & Greenspan DC (1997) Occlusion of dentin tubules by 45S5 Bioglass. In: Bioceramics Vol. 10 Proceedings of the 10th International Symposium on Ceramics in Medicine *Elsevier Scientific* 411-414.
11. Forsback AP, Areva S, & Salonen JI (2004) Mineralization of dentin induced by treatment with bioactive glass S53P4 in vitro *Acta Odontologica Scandinavica* **62(1)** 14-20.
12. Vollenweider M, Brunner TJ, Knecht S, Grass RN, Zehnder M, Imfeld T, & Stark WJ (2007) Remineralization of human dentin using ultrafine bioactive glass particles *Acta Biomaterials* **3(6)** 936-943.
13. Sauro S, Watson TF, Mannocci F, Tay FR, & Pashley DH (2009) Prevention of water contamination of ethanol-saturated dentin and hydrophobic hybrid layers *Journal of Adhesive Dentistry* **11(4)** 271-8.
14. Pashley DH (1996) Dynamics of the pulpo-dentin complex *Critical Reviews in Oral Biology and Medicine* **7(2)** 104-133.
15. Sauro S, Watson TF, & Thompson I (2010) Dentine desensitization induced by prophylactic and air-polishing procedures: an in vitro dentine permeability and confocal microscopy study *Journal of Dentistry* **38(5)** 411-422.
16. Pashley DH & Depew DD (1986) Effects of smear layer, copalite and oxalate on microleakage *Operative Dentistry* **11(3)** 95-102.
17. Hench LL & Andersson Ö (1993) Bioactive glasses. In: Hench LL, Wilson J (eds) *Introduction to Bioceramics* World Scientific, Singapore 45-47.
18. Paolinelis G, Banerjee A, & Watson TF (2008) An in vitro investigation of the effect and retention of bioactive glass air-abrasive on sound and carious dentine *Journal of Dentistry* **36(3)** 214-218.
19. Tsuda H, Ruben J, & Arends J (1996) Raman spectra of human dentin mineral *European Journal of Oral Science* **104(2, Part 1)** 123-131.
20. Tsuda H & Arends J (1997) Raman spectroscopy in dental research: A short review of recent studies *Advances in Dental Research* **1(4)** 539-547.
21. Gandolfi MG, Silvia F, H PD, Gasparotto G, & Carlo P (2008) Calcium silicate coating derived from Portland cement as treatment for hypersensitive dentine *Journal of Dentistry* **36(8)** 565-578.
22. Andersson OH & Kangasniemi I (1991) Calcium phosphate formation at the surface of bioactive glass in vitro *Journal of Biomedical Materials Research* **25(8)** 1019-1030.
23. Hench LL & Andersson Ö (1993) Bioactive glasses. In: Hench LL, Wilson J (eds) *Introduction to Bioceramics* World Scientific, Singapore 45-47.
24. Cerruti MG, Greenspan D, & Powers K (2005) An analytical model for the dissolution of different particle size samples of Bioglass in TRIS buffered solution *Biomaterials* **26(24)** 4903-4911.

Dentinal hypersensitivity and the science of Sylc

Aran Batth, Julian Zeolla, Hannah Gorgui-Naguib and **Ian Thompson** investigate how bioactive glass can help dentists combat sensitivity

The aetiology of dentinal hypersensitivity (DH) is multi-factorial and not completely understood, although it has been demonstrated that the structure of dentine in the affected areas is altered, containing a larger number of patent dentine tubules than unaffected areas (Absi et al 1987).

Yoshiyama et al (1989 and 1990) reported that a greater proportion of the tubules were patent in the sensitive areas and noted the presence of tubule–like structures situated superficially beneath the surface of sensitive dentine.

Not all exposed dentine, however, is sensitive; evidence from SEM investigation of extracted teeth would suggest that there are differences between 'sensitive' and 'non-sensitive' dentine in that there are more open dentinal tubules (with a greater mean orifice diameter) in sensitive dentine (Absi et al 1987).

According to Gillam (2009), these findings appear to be consistent with Brännström's 1963 hydrodynamic theory of stimulus transmission across dentine (1984). This theory proposes that minute rapid shifts (in either direction) of the fluid within the dentine tubules (following stimulus application) may result in activation of the sensory nerves in the pulp/inner dentine region of the tooth.

Aran Batth is a research fellow at King's College London

Julian Zeolla is a research fellow at King's College London

Hannah Gorgui-Naguib is a research fellow at King's College London.

Dr Ian Thompson is a senior lecturer at King's College London and the product director of Denfotex Research.

CPD

Education aims and objectives

This article aims to describe some of the currently understood causes and mechanisms of dentinal hypersensitivity and discuss some of the proposed treatments.

Expected outcomes

Correctly answering the questions of page 54, worth one hour of verifiable CPD, will demonstrate that the reader understands the causes and mechanisms of dentinal hypersensitivity and how bioactive glass plays a part in possible treatment for it.

Methods of desensitisation

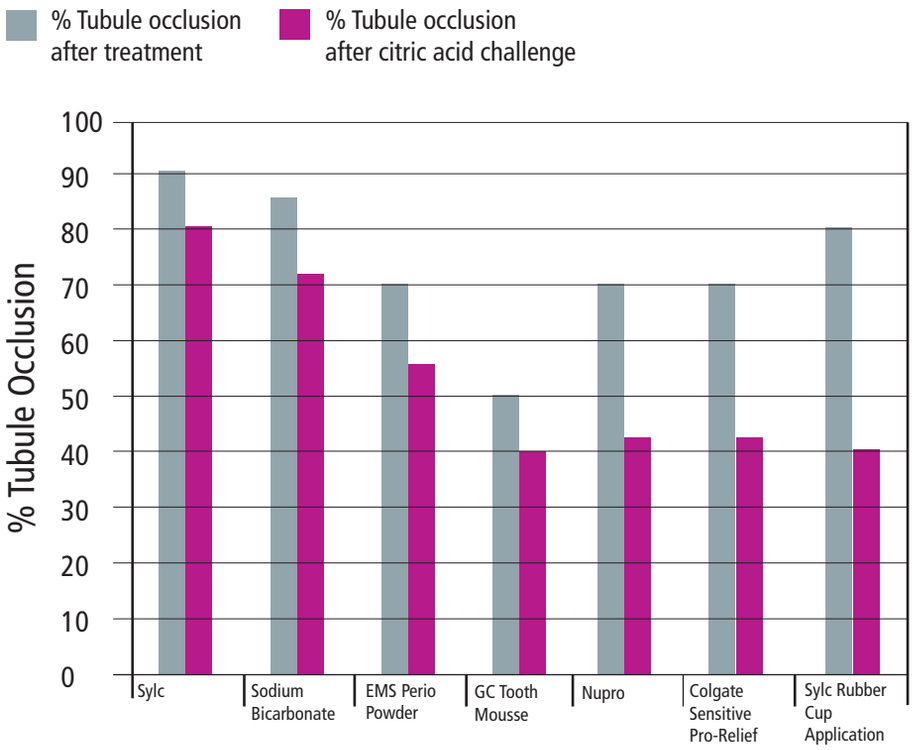
Currently there are two main approaches for the treatment of DH based on the hydrodynamic theory. Namely, these are:

1. Tubule occlusion
2. Blocking nerve activity through direct ionic diffusion (increased potassium ions concentration acting on the pulpal sensory nerve activity) (Berkstein et al 1987).

Banerjee and colleagues (2010) suggest that there are many approaches to the treatment and prevention of dentinal hypersensitivity.

Treatment of the tooth with a chemical agent, which penetrates into the dentinal tubules and depolarises the nerve synapse, reducing sensitivity by preventing the conduction of pain impulses, is a method used in daily use toothpastes (eg potassium nitrate) (Markowitz and Kim 1992; Schiff et al 1998).

An alternative approach is to treat the tooth with a chemical or physical agent, which creates a layer that mechanically occludes the exposed dentinal tubules, thus reducing sensitivity by preventing dentinal fluid flow – a method used by prophylaxis pastes and varnishes (eg potassium oxalate, ferric oxalate)



(Orchardson and Gillam 2000; Dragolich et al 1993).

Although both approaches are effective at reducing or eliminating hypersensitivity, the duration of the relief is variable. Dentine hypersensitivity usually re-occurs due to abrasion from excessive tooth brushing, chemical erosion or mechanical failure of the coating material (Kozlovsky et al 1989).

Uses of bioactive glass

Consequently dental materials are needed that can chemically react with tissues, so significantly reducing the possibility of reopening occluded tubules.

Progress has been made towards meeting this need through the development of materials that deposit calcium phosphate onto the tooth surface to mechanically occlude exposed dentinal tubules.

Commercially available products such as NovaMin (GSK, UK) provide such ions for remineralisation. Additional technologies, but with a differing mechanism of action, such as Tooth Mousse (GC, USA) provide a source of calcium for surface remineralisation (Reynolds 1987; Featherstone et al 1992; Du Min et al 2008).

More recently bioactive glass, Sylc, has been used in a series of therapeutic prophy powder that provides four treatments in one application. It has proven to clean and polish, decreases dentinal hypersensitivity, uniquely repairs dental tissues and brightens teeth to a natural whiteness.

Sylc as a desensitising system

A number of studies on the desensitising properties on bioactive glass have been conducted and published. Banerjee et al (2010) found that Sylc air polishing was more clinically and statistically effective at desensitising teeth in both good and poor hygiene groups than sodium bicarbonate. Sylc also provided better overall patient comfort during the procedure. Furthermore, Banerjee and colleagues also demonstrated that the bioactive glass powder had a significant longer-term desensitising effect compared to other powders

The experiments performed in this study showed a substantially higher dentine desensitisation induced by Sylc powder compared to the other materials; Cavitron Prophy-Jet (Dentsply, USA), Air-flow powder Perio (EMS, Switzerland), GC Tooth Mousse (GC, Japan), Colgate Sensitive Pro-Relief (Colgate Palmolive, UK) and Nupro with Bioactive glass (Dentsply, USA).

When the Sylc material was applied via slightly damp rubber cup, the level of tubule occlusion was significantly higher than that of the other air polishing powders (Table 1).

Care to comment? @AesDenToday

References

Absi EG, Addy M, Adams D (1987). Dentine hypersensitivity. A study of the patency of dentinal tubules in sensitive and non-sensitive cervical dentine. J Clin Periodontol 14: 280-4

Banerjee A, Hajatdoost-Sani M, Farrell S, Thompson I (2010). A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air polishing powders. J Dent 38: 475 – 479

Berkstein S, Reiff RL, McKenney JF, Kilroy WJ (1987): Supragingival root surface removal during maintenance procedures utilizing an air-powder abrasive system or hand scaling; J Periodontol 58: 327-330

Dragolich WE, Pashley DH, Brennan WA, O'Neal RB, Horner JA, Van Dyke TE (1993). An in vitro study of dentinal tubule occlusion by ferric oxalate. Journal of Periodontology 64: 1045-52

Du Min Q, Bian Z, Jiang H, Greenspan DC, Burwell AK, Zhong J (2008). Clinical evaluation of a dentifrice containing calcium sodium phosphosilicate (NovaMin) for the treatmenet of dentin hypersensitivity. American Journal of Dentistry 21: 210-214

Featherstone JDS et al (1992). An in situ model for simultaneous assessment of inhibition of demineralization and enhancement of remineralisation. Journal of Dental Research 71: 804-810

Gillam D (2009). Making sense of dentine hypersensitivity; Dental Practice July: 10-11

Kozlovsky A, Soldinger M, Sperling I (1989). The effectiveness of the air-powder abrasive device on the tooth and periodontium: an overview. Clinical Prevention in Dentistry 11: 7-11

Markowitz K, Kim S (1992). The role of selected cations in the desensitization of intradental nerves. Proceedings of the Finnish Dental Society. 88: 39-54

Orchardson R, Gillam D (2000). The efficacy of potassium salts as agents for creating dentin hypersensitivity. Journal of Orofacial Pain 14: 9-19

Reynolds EC (1987). The prevention of sub-surface demineralization of bovine enamel and change in plaque composition by casein in an intra-oral model. Journal of Dental Research 66: 1120-7

Schiff T, Dos Santos M, Laffi S, Yoshioka M, Baines E, Brasil KD (1998). Efficacy of dentifrice containing 5% potassium nitrate and 1500 ppm sodium monofluorophosphate in a precipitated calcium carbonate base on dentinal hypersensitivity. J Clin Dent. 9: 22-25

Weaks LM, Lescher NB, Barnes CM, Holroyd SV (1984). Clinical evaluation of the prophy-jet as an instrument for routine removal of tooth stain and plaque. J Periodontol 55: 486-488

Yoshiyama M, Masada J, Uchida A, Ishida H (1989). Scanning electron microscopic characteristics of sensitive vs. insensitive human radicular dentin. J Dent Res 68: 1498-1502

Yoshiyama M, Noiri Y, Ozaki K, Uchida A, Ishikawa Y, Ishida H (1990). Transmission electron microscopic characterization of hypersensitive human radicular dentin. J Dent Res 69: 1293-7

Bioactive glass as a tooth remineralisation agent

Aran Batth, Julian Zeolla, Hannah Gorgui-Naguib and **Ian Thompson** investigate the role of Sylc in remineralising tooth structure

As teeth are exposed to biofilm-related organic acid production, the rate of demineralisation of carbonated hydroxyapatite exceeds that of remineralisation by ions contained within the saliva (Featherstone, 2008; Banerjee et al, 2010). This imbalance results in exposed dentinal tubules, leading to hypersensitivity.

Hypersensitivity is prevalent within the UK, having been reported to affect 4% of the population.

Aran Batth is a research fellow at King's College London

Julian Zeolla is a research fellow at King's College London

Hannah Gorgui-Naguib is a research fellow at King's College London

Ian Thompson is a senior lecturer at King's College London and the product director of Denfotex Research

CPD

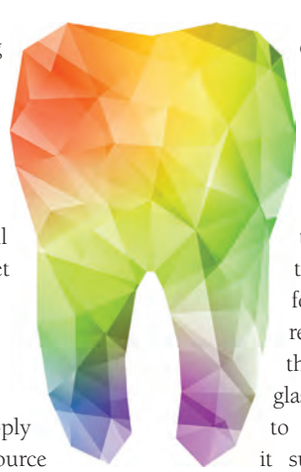
Education aims and objectives

This article aims to explain how bioactive glass can help remineralise teeth and reduce hypersensitivity.

Expected outcomes

Correctly answering the questions on page 50, worth one hour of verifiable CPD, will demonstrate that the reader understands the mechanisms involved in the remineralisation of tooth structure by bioactive glasses.

Various remineralising vehicles – including topical fluoridation, casein phosphopeptide-amorphous calcium phosphate formation and bioactive glasses –have been employed to address this clinical issue (Pizzo et al, 2007; Wang et al, 2011).



An introduction to bioactive glass

Bioactive glass acts to supply biologic material with the source of calcium and phosphates contained within its silicate frame (Hench and Wilson 1993), in the same proportion to hydroxyapatite.

In an aqueous environment the glass reacts in dissolution of the phosphates and calcium to form hydroxycarbonate apatite, resultant in adhesion of cells to the glass. The safety of bioactive glass has been assayed and shown to be adequate in vivo making it suitable for clinical application

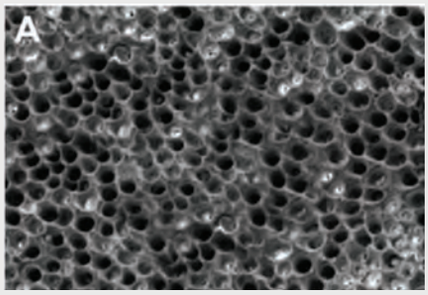


Figure1a: 1000x SEM micrograph – exposed dentinal tubules after H3PO4 application

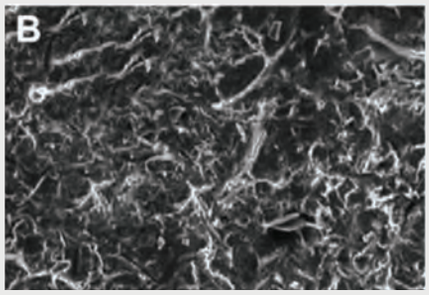


Figure1b: 1000x SEM micrograph – Sylc bioactive glass powder applicational effects, result in smeared layers on surface occluding dentinal tubules. (Sauro, 2011)

(Hench and Wilson 1993).

Sylc bioactive glass can be employed for use in combatting dental hypersensitivity or remineralising the resin-dentine interface prior to air-cutting procedures – giving great clinical scope for the Sylc products (Suaro et al, 2011).

Sylc as a remineralisation agent

Bioactive glass leads to increased of tubular occlusion in vitro. It is a biomaterial extensively used in tissue engineering, bone regeneration and dentine remineralisation due to its process of hydroxycarbonate apatite formation (Litkowski et al, 1997).

Tubular occlusion by use of Sylc results in island formation of calcium phosphate and smearing across the dentine border (Figure 1) (Suaro et al, 2011).

Reacting with a salivary environment, the active ingredient of Sylc – Novamin – releases calcium and phosphate ions (Burwell et al, 2009). The ions integrate into the dentine structure to reintroduce a remineralised framework to the tooth interface.

This is achieved by precipitation of a phosphate-based analogue to hydroxyapatite, which is functional as a protective barrier to oral acidity (Earl et al, 2011; Mehta et al, 2014).

Data

When compared to other test materials (Prophy Powder and EMS Perio), Sylc bioactive glass is shown by Raman Spectroscopy to produce peaks that indicate hydroxycarbonate apatite formation and thus remineralisation (Sauro et al, 2011).

An interaction between dentine and bioactive glass results in leaching of materials through salivary submergence, shown in vitro by (Efflandt et al, 2002; Paolinelis et al, 2007). Through an active process of mineral release from the glass complexes; recovery from a demineralised state has been shown through X-ray diffraction studies in the form of apatite growth and mineral elements observed (Wang et al, 2011).

Summary

The Sylc range of products offers a diversity of use, predominately downstream of the particulate's ability to remineralise dentine. After treatment with bioactive glass (Sylc), tooth dentine surface is protected by a smear of crystallised hydroxyapatite-like material. Such remineralisation can restore a mineral balance to the tooth structure, reduce hypersensitivity and offers caries protection.

Care to comment? @AesDenToday

References

Banerjee A, Hajatdoost-Sani M, Farrel S, Thompson I (2010). A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air-polishing powders. Journal of Dentistry 38: 475-479

Burwell A, Litkowski L, Greenspan D (2009). Calcium Sodium Phosphosilicate (NovaMin): Remineralization Potential. Advances in Dental Research 21: 35-39

Earl J, Leary R, Muller K, Langford R, Greenspan D (2011). Physical and chemical characterization of dentin surface following treatment with NovaMin technology. Journal of Clinical Dentistry 2(3): 62-7

Efflandt S, Magne P, Douglas W, Francis L (2002). Interaction between bioactive glasses and human dentin. Journal of Material Science 13: 557-565

Featherstone J (2008). Dental caries: A dynamic disease process. Australian Dental Journal 53(3): 286-291

Hench L, Wilson J, eds (1993). An introduction to bioceramics. World Scientific Publishing, Singapore

Litkowski L, Hack G, Sheaffer H, Greenspan D (1997). Occlusion of Dentine Tubules by 45S5. Bioceramics 10

Mehta A, Kuman V, Jose R, Izadikhah V (2014). Remineralization potential of bioactive glass and casein phosphopeptide-amorphous calcium phosphate on initial carious lesion: An in-vivo pH-cycling study. Journal of Conserv Dent, 17(1), pp. 3-7.

Paolinelis G, Banerjee A, Watson T (2007). An in vitro investigation of the effect and retention of bioactive glass air-abrasive on sound and carious dentine. Journal of Dentistry 36: 214-218

Pizzo P, Piscopo M, Pizzo I, Giuliana G (2007). Community water fluoridation and caries prevention: a critical review. Clinical Oral Investigations 11(3): 189-193

Sauro S, Thompson I, Watson T (2011). Effects of Common Dental Materials used in Preventative or Operative Dentistry on Dentin Permeability and Remineralisation. Operative Dentistry 36(2): 222-230

Wang Z, Jiang T, Sauro S, Pashley D, Toledano M, Osorio R, Liang S, Xing W, Sa Y, Wang Y (2011). The dentine remineralization activity of a desensitizing bioactive glass-containing toothpaste: an in vitro study. Australian Dental Journal 56: 372-381

Wang Z, Jiang T, Sauro S, Wang Y, Thompson I, Watson T, Sa Y, Xing W, Shen Y, Haapasalo M (2011). Dentine Remineralisation induced by two bioactive glasses developed for the air abrasion purposes. Journal of Dentistry

sylc® Therapeutic Prophy Powder

POWERED BY **NOVAMIN®**

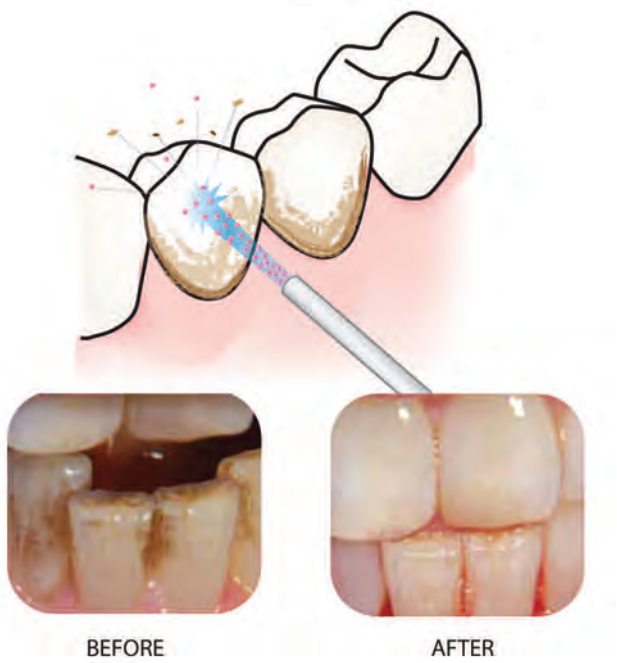
What does it do?

High level, Fast cleaning[1,2,3]

Fast Desensitizing[4]

Increased Patient Comfort[5]

Protect and Soothe[6,7]



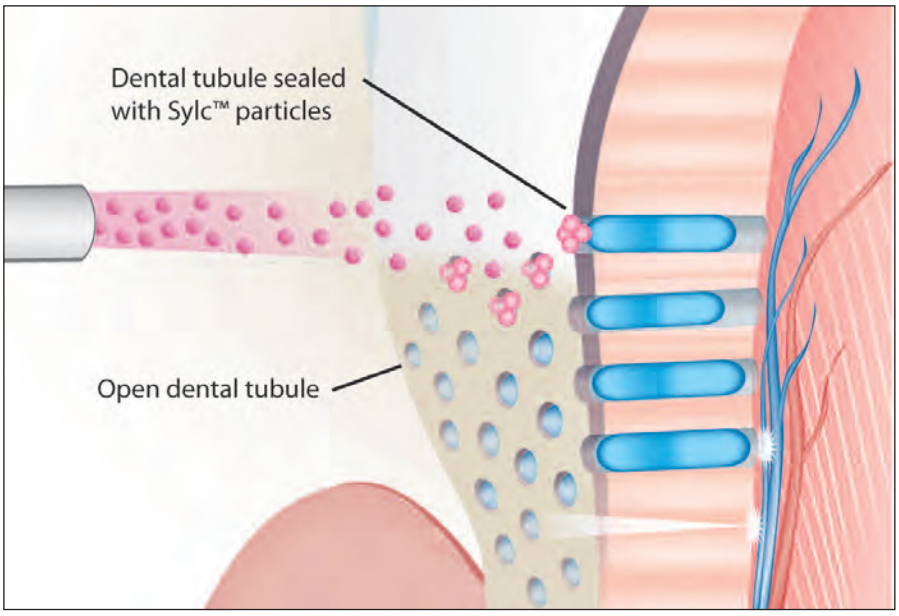
How does it work?

Sylc's protective and soothing ability comes from Novamin.

NovaMin is calcium sodium phosphosilicate, which seeks out and forms a tooth-like layer over vulnerable areas of the tooth where dentine is exposed.

When combined with saliva or water, Sylc forms hydroxycarbonate apatite crystals (HCA) that increase the natural protective and repair mechanisms of saliva.

Unlike traditional desensitising varnishes or pastes, Sylc provides superior relief from painful hypersensitivity without unsightly discolouration or unpleasant taste or feel.



Illustrations are interpretive depictions for informational purposes only.