Comparison between the Efficacy of Novamin™ and Pro-argin™ Toothpastes in Dentin Permeability

การเปรียบเทียบประสิทธิผลของยาสีฟันที่มี Novamin™ และ Pro-Argin™ ต่อการซึมผ่านของของเหลวทางท่อเนื้อฟัน

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ABSTRACT

Aims: To compare the efficacy of Novamin™ and Pro-Argin™ toothpastes on dentin permeability. Material and Methods: Sixty dentin discs from third molars were etched with EDTA for 24 hours, then brushed with toothpastes containing fluoride, Novamin™ or Pro-argin™. Dentin permeability was measured before and after brushing. Other 5 discs were used to determine dentinal tubule occlusion using SEM. Results: Dentin treated with 3 toothpastes created tubule occlusion. The percentage reduction of dentin permeability were 39.26, 32.27 and 21.71 for groups of Pro-argin™, Novamin™ and fluoride, respectively. Only the difference in percentage reduction between Pro-argin™ and fluoride groups was significant. Conclusion: All 3 products occluded dentinal tubules and reduced dentin permeability. The single-use of Pro-argin™ toothpaste was more effective in reducing dentin permeability than fluoride toothpaste.

บทคัดย่อ

วัตถุประสงค์: เพื่อเปรียบเทียบประสิทธิผลของยาสีฟันที่มี Novamin™ และ Pro-Argin™ เป็นส่วนประกอบในการลดการซึมผ่านของของเหลวผ่านท่อเนื้อฟัน วัสดุและวิธีการ: นำแผ่นเนื้อฟัน 60 ชิ้นจากฟันกรามซี่ที่สาม แช่ในสารละลายอีดีทีเอ 24 ชั่วโมง และแปรงด้วยยาสีฟันที่มีฟลูออไรด์ Novamin™ หรือ Pro-Argin™ แล้ววัดการซึมผ่านของของเหลวก่อนและหลังแปรง แผ่นเนื้อฟันอีก 5 ชิ้น วัดการอุดตันของท่อเนื้อฟันด้วยกล้องจุลทรรศน์อิเล็กตรอนแบบส่องกราด ผล: ผลิตภัณฑ์ทั้ง 3 ชนิดอุดตันท่อเนื้อฟันและร้อยละของการลดการซึมผ่านของของเหลวคือ 39.26, 32.27 และ 21.71 ในกลุ่ม Pro-Argin™ Novamin™ และฟลูออไรด์ตามลำดับ โดยยาสีฟันที่มี Pro-Argin™ ลดการซึมผ่านของของเหลวได้มากกว่ายาสีฟันฟลูออไรด์อย่างมีนัยสำคัญ สรุป: ยาสีฟันทั้ง 3 ชนิดสามารถอุดตันและการลดการซึมผ่านของของเหลวได้ โดยยาสีฟันที่มี Pro-Argin™ มีประสิทธิผลมากกว่ายาสีฟันที่มีฟลูออไรด์หลังแปรงเพียง 1 ครั้ง

Keywords: Dentin hypersensitivity, Novamin™, Pro-Argin™

คำสำคัญ: อาการเสียวฟัน โนวามิน™ โปร-อาร์จิน™

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Introduction

Dentin hypersensitivity is most common complaints of individuals seeking for dental treatments. The prevalence of dentin hypersensitivity ranges from 4% to 57% (Cummins, 2010) and increases to 62.5% to 90% following periodontal therapy (Lin and Gillam, 2012). It is characterized by short and sharp pain which responds to external stimuli on exposed dentin typically thermal, air spray, tactile, osmotic or chemical stimuli which cannot be recognized by any other forms of dental defects or diseases. The common causes of exposed dentin are gingival recession and enamel loss from improper tooth brushing or periodontal disease progression and its treatment (Addy, 2002; Canadian Advisory Board on Dentin Hypersensitivity, 2003; Markowitz and Pashley, 2008).

The mechanism of dentin hypersensitivity was described by Brännström (Brännström, 1966). Starting from, external stimuli on exposed dentin induce movement of dentinal fluid, change pressure across dentin which activates intra-pulpal nerve fibers then causes pain (Addy, 2002; West, 2006). The finding from scanning electron microscopy (SEM) showed that higher numbers as well as larger sizes of dentinal tubules were detected in sensitivity teeth which consequently elevate fluid flow rate in sensitivity teeth (Absi et al., 1987; Absi et al., 1989; Addy, 2002).

For treating dentin hypersensitivity, a number of dental products were developed basically based on two distinct approaches: (i) Interruption of neural response to pain stimulus or (ii) Occlusion of exposed and open dentinal tubules to block hydrodynamic mechanism of pain stimulation.

Recently, new materials have been developed to induce the formation of a dentin-like layer which resists to mechanical and chemical stimuli by sealing and blocking exposed tubules. So far, this method shows more effective in reducing dentin hypersensitivity than neural interrupting method.

Calcium sodium phosphosilicate, commercially called "Novamin™" was first introduced for in-office use in mid-1990s. When calcium sodium phosphosilicate contacts with saliva, it releases calcium and phosphate ions then form hydroxyapatite crystals to seal and block exposed dentinal tubules. Moreover, residual calcium sodium phosphosilicate particles can block tubules as well (Rajesh et al., 2012). An *in-vitro* study showed Novamin™ containing toothpaste can create a hydroxyapatite-like layer to seal dentinal tubules of a dentin disc (Earl et al., 2011) and the blockade is more stable than that of silica-containing toothpaste. Furthermore, the Novamin™ toothpaste also reduce dentin permeability (Wang et al., 2010). A clinical study showed that the Novamin™ toothpaste was more effective than strontium-based and placebo toothpastes in reducing dentin hypersensitivity following the 6-week use. (Du et al., 2008).

The later, arginine calcium carbonate which is commercially called "Pro-argin™" is a new substance developed in mid-1990s similarly to Novamin™. Arginine and calcium which have positive charges in physiologic pH bind to dentin surfaces in turn form a calcium-rich layer for sealing and blocking exposed dentinal tubules (Kleinberg, 2002). An *in-vitro* study showed that the Pro-argin™ toothpaste blocked or narrowed dentinal tubules of a dentin disc after brushing for 2 minutes and the

blockade was more stable than that of strontium chloride-containing toothpaste (Li et al., 2012). Moreover, Pro-argin™ toothpaste reduced dentin permeability more effective than strontium acetate toothpaste did (Patel et al., 2011). Clinical studies also showed similar results on reducing dentin hypersensitivity after use for 2-, 4- and 8-weeks (Ayad et al., 2009a; Docimo et al., 2009). Furthermore, an instant relief of dentin hypersensitivity after single application Pro-argin™ on sensitive dentin has been reported (Ayad et al., 2009b).

Until now, the evidence in the comparison between the efficacy of Novamin™ and Pro-Argin™ on dentin hypersensitivity is still limit. Mostly, several studies focused on the efficacy of dentinal tubule occlusion but lack of data to support the effect of these two products on dentin permeability. Therefore, this study aimed to compare the efficacy of Novamin™ and Pro-Argin™ containing toothpastes on dentin permeability and dentinal tubule occlusion which may contribute to further develop guideline on the use of these products in treating dentin hypersensitivity.

Objectives of the study

1. To compare between the efficacy of Novamin™ and Pro-Argin™ toothpastes in dentinal tubule occlusion.

2. To compare between the efficacy of Novamin™ and Pro-Argin™ toothpastes in dentinal permeability.

Methodology

Dentin sample preparation

Sixty-five extracted third molars were collected after the study protocol approved by the Human Research Ethics Committee of the Faculty of Dentistry, Chulalongkorn University (HREC-DCU2015-054). Teeth were cleaned and stored in 1% thymol.

Dentin specimens were cut perpendicular to long axis above the cemento-enamel junction to create 1 mm-thick dentin disc by a low-speed water cooled diamond saw (Isomet®1000). Each dentin disc was prepared and examined to assure that the specimen was free of coronal enamel and no pulpal exposure.

SEM analysis

Five dentin discs were used to evaluate dentinal tubule occlusion. Each dentin disc was etched with 0.5 M ethylenediamine tetra-acetic acid (EDTA) for 24 hours, then split into 4 pieces for:

- No treatment (as baseline).
- Brush with the fluoride toothpaste for 1 minute.
- Brush with the Novamin™ toothpaste for 1 minute.
- Brush with the Pro-Argin™ toothpaste for 1 minute.

After that, each specimen was air-dried at room temperature. A scanning electron microscope was used to examine dentin disc morphology.

Experimental design

Sixty dentin discs were soaked in 0.5 M EDTA for 24 hours to remove the smear layer and smear plug. The etched disc was rinsed and kept moist to evaluate the maximum permeability (100% permeability). Next, dentin discs were randomly assigned to 3 groups of 20 dentin discs. The dentin disc was then soaked with artificial saliva and brushed with fluoride toothpaste for 1 minute as a

control. While test groups were brushed with either NovaMin™ or Pro-Argin™ toothpastes.

The permeability of each dentin disc was re-measured and results were presented as the percentages of maximum EDTA-etched permeability. (Wang et al., 2011)

Dentin permeability measurement

Dentin permeability measurement system was set as shown in Figure 1. A dentin disc (1) was placed tightly between double rubber "O" rings (2), which had surface area approximately 0.78 cm^2 for filtration of water. The upper "O" ring was covered with the glass slab to seal the system and the lower "O" ring was connected to the water-filled system at 20 cm H_20 (3), which mimics the pulpal pressure. An air bubble was introduced into the water-filled system by a syringe (4). Then, the dentin permeability of a dentin disc was determined by measuring the duration of the movement of air bubble through the capillary tube (5). The duration of the movement of bubble was converted to hydraulic conductance (Lp) for each dentin disc, by dividing the fluid flow (Jv) by the exposed dentin surface area (A) and water pressure (P) (Pashley *et al.,* 1996).

$$Lp = Jv/A(P)$$

Jv; fluid flow (µL/min), A; surface area for fluid filtration (cm^2) and P; pressure (cm H_2O)

The percentages (%Lp) of dentin permeability were calculated. The mean percentage reduction (%Lp) between before and following brushing on the same disc was considered as the efficacy in reducing dentin permeability of each group.

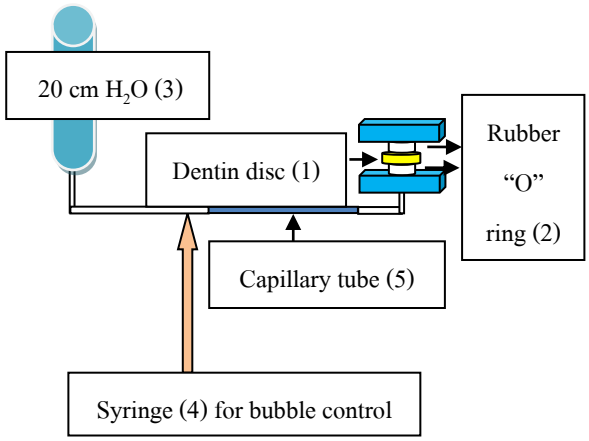

Figure 1 Dentin permeability measurement system.

Statistical analysis

The data were analyzed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Results were presented in median (range). The non-parametric Kruskal-Wallis test was used to determine the difference of percent reduction of dentin permeability among 3 groups. A p-value less than 0.05 was considered as statistically significant.

Results

SEM evaluation

SEM results showed in Figure 2. The left panel showed dentin surfaces at 2000X and the right panel showed dentinal tubule orifices in higher magnification (10000X).

After EDTA etched for 24 hours, dentin surfaces were free from the smear layer and smear plug (Fig. 2A). Most of dentinal tubules were completely open (Fig. 2B). Dentin treated with fluoride toothpaste exhibited fine debris on dentin surfaces however most of tubules were still open (Fig. 2C, D). Dentin treated with Novamin™ toothpaste showed a large amount of deposits on both dentin surfaces and orifices of dentinal tubules (Fig. 2E, F). Dentin treated with Pro-argin™ toothpaste seemed to show larger amount of deposits on dentin surfaces

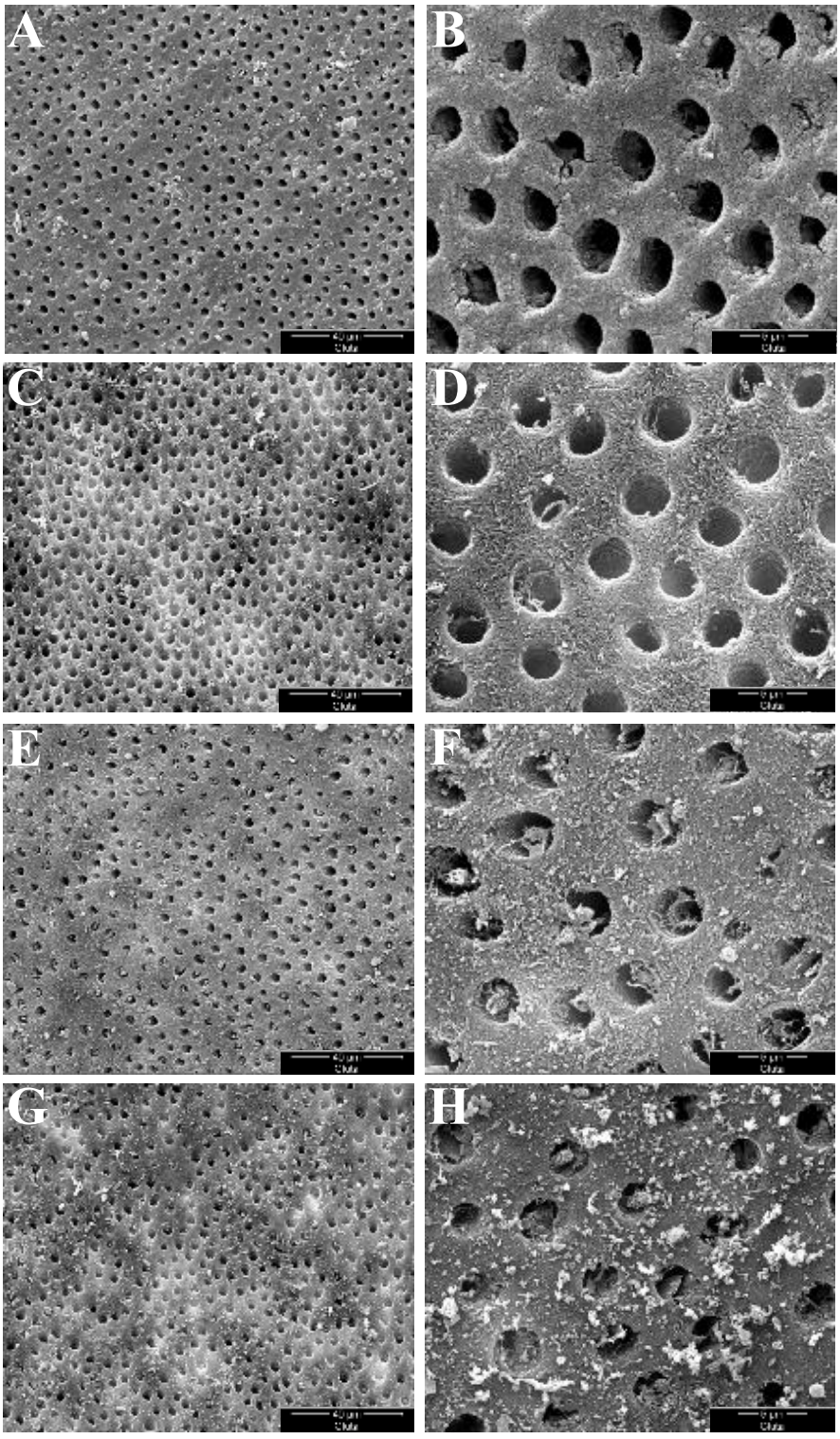

Figure 2 SEM images of dentin surface morphology at 2000X (left) and 10000X (right). Each dentin disc was etched with EDTA for 24 hours (Fig. 2A and B) and then brushed for 1 minute with fluoride (Fig. 2C and D), Novamin™ (Fig. 2E and F) or Pro-argin™ (Fig. 2G and H) toothpastes.

and orifices of dentinal tubules than Novamin™ and fluoride toothpastes. In addition, at a high magnification, complete occlusion was observed in Pro-argin™ group (Fig. 2G, H).

Dentin permeability measurement

The decreased hydraulic conductance (Lp) following brushing in all 3 groups indicated the reduction of dentin permeability (Table 1).In addition, the differences of Lp values before and following brushing with fluoride, Novamin, Pro-argin toothpastes were statistically significant.

Table 1 Lp data before (Pre Tx) and following brushing (Post Tx) dentin discs with fluoride, Novamin™, Pro-argin™ containing toothpastes. Values were shown in median (range).

	Pre Tx	Post Tx	p-value
Fluoride	0.17 (0.02-1.46)	0.10 (0.01-0.93)	0.0001*
NovaMin™	0.14 (0.01-1.91)	0.12 (0.01-0.95)	0.0001*
Pro-argin™	0.18 (0.02-0.96)	0.11 (0.01-0.50)	0.0001*

* Compared between pre- and post- treatment of each group.

The percentage reduction of dentin permeability after using 3 different toothpastes were calculated from reduction of 100% permeability of EDTA-etched showed in table 2. After brushing for 1 minute, Pro-argin™ seemed to show the highest potential reduction of dentin permeability (Lp ~39.26%). Novamin™ and fluoride toothpaste uses were able to reduce dentin permeability but the degrees of reduction (32.27% and 21.71%, respectively) were probably inferior to that of Pro-argin™. The difference in percentage reduction of dentin permeability among 3 toothpastes was statistically significant. Furthermore, when compared between groups, Pro-argin™ exhibited more effective in reducing dentin permeability than fluoride toothpaste ($p = 0.0119$). However, the differences on the percentage reduction of dentin permeability between fluoride and NovaMin™ groups as well as between NovaMin™ and Pro-argin™ groups were not statistically significant (Table 2, Figure 3).

Table 2 Dentin permeability reductions. Values (expressed as %) were shown in median (range).

	Fluoride	Novamin™	Pro-argin™
EDTA	100	100	100
Tooth brushing	78.29 (48.49-99.46)	67.73 (10.10-88.23)	60.74 (19.17-91.78)
%reduction	21.71** (0.54-51.51)	32.27 (11.77-89.90)	39.26** (8.22- 80.83)

** Compared the reduction of dentin permeability between groups.

Discussion

Nowadays, several methods have been introduced for treating dentin hypersensitivity. The traditional approach is to occlude dentinal tubules then block pain mechanism following hydrodynamic concept. The uses of Novamin™ and Pro-Argin™ are current technologies that have been developed to induce the formation of dentin-like layers for sealing and blocking exposed dentinal tubules in turn reduce dentin hypersensitivity. This

study aimed to compare the efficacy in reducing dentin permeability and dentinal tubule occlusion following Novamin™ and Pro-Argin™ containing toothpaste use.

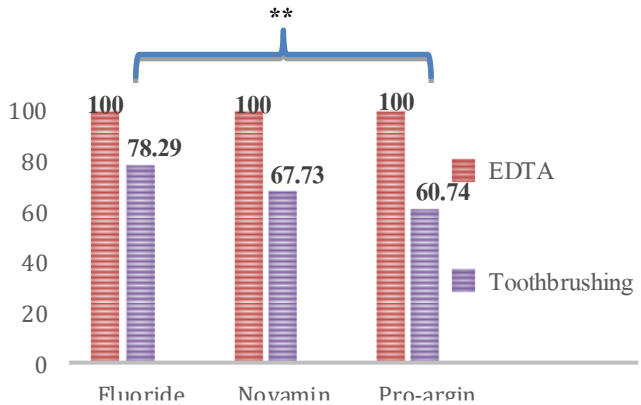

Figure 3 Percentage reduction of dentin permeability following treatments.

** Compared percentage reduction of dentin permeability between fluoride and Pro-argin™ groups.

The SEM results was in agreement with previous studies which showed tooth brushing can create dentinal tubule occlusion. However, the degrees of tubule occlusion depend on active ingredients available in each toothpaste (Rajesh et al., 2012; Earl et al., 2011; Wang et al., 2010; Kleinberg, 2002; Li et al., 2012; Patel et al., 2011). Markowitz and Pashley described that hydraulic conductance depended on numbers and diameters of dentinal tubules, therefore the reduction of patent dentinal tubules could decrease dentin permeability (Markowitz and Pashley, 2008). This finding implies that the more tubules are occluded, the more dentin permeability are possibly reduced.

The evidence from both *in-vitro* and *in-vivo* confirmed that Novamin™ and Pro-argin™ have higher ability in blocking dentinal tubules as well as reducing dentin permeability than other available desensitizing agents (Earl et al., 2011; Li et al., 2012). Our study showed that fluoride toothpaste may have the lowest effect on blocking of dentinal tubules and reducing dentin permeability similarly to previous report.

The percentage reduction of dentin permeability were 39.26, 32.27 and 21.71% following using Pro-argin™, Novamin™ and fluoride toothpastes, respectively. Even though, the difference in percentage reduction of dentin permeability n between Novamin™ and Pro-argin™ groups was not statistically significant, our study is the first report in the comparison between the efficacy of Novamin™ and Pro-argin™ usages.

Even though, our SEM results shows some deposits and occluded dentinal tubules following Novamin™ and Pro-argin™ treatments, the amount of deposits and occluded tubules were lesser than those of previous studies (Wang et al., 2010; Li et al., 2012). Wang and colleagues showed almost completely occluded dentinal tubules after a single use of Novamin™ toothpaste (Wang et al., 2010). While Li and colleagues showed the same result after applied Pro-argin™ twice daily for 4 days (Li et al., 2012). The differences of degree of dentinal tubule occlusion may be explained by different treatment protocols. Our protocol was brushing 1 minute with soft brush while the former protocol was brushing 2 minutes with medium hardness brush (Wang et al., 2010). The increasing time of brushing is possibly increasing chance for Novamin™ to react with saliva then create dentin-like structure for blocking tubules. Similarly, increased exposure time of Pro-argin™ for 4 days also induced more dentin-like structure on the dentin disc. (Li et al., 2012).

Our dentin permeability result also showed lesser percentage reduction of dentin permeability following Novamin™ (Wang et al., 2010) and Pro-argin™ use (Patel et al., 2011). The reason is probably due to distinct of brushing protocols as describe earlier. However, no previous evidence reported on the comparison between the efficacy of Novamin™ and Pro-argin™ toothpastes in reducing dentin permeability.

A clinical study showed no difference in reduction of dentin hypersensitivity between Novamin™ and Pro-argin™ toothpastes after single use (Rao et al., 2014). However, Novamin™ showed significantly more reduction of dentin hypersensitivity after 15-day follow up when compared with Pro-argin™ (Rao et al., 2014). In contrast, another study showed that Pro-Argin™ was more effective in reducing dentin hypersensitivity than that of Novamin ™after 2-, 4- and 8- weeks use (Docimo et al., 2011). Since this study evaluated the efficacy of these toothpastes following single-use, a further study on longer term used of these toothpastes needs to be conducted.

Conclusion

All 3 toothpastes including Pro-argin™, Novamin™ and fluoride containing toothpastes, occluded dentinal tubules and reduced dentin permeability. Among three toothpastes, only Pro-argin™ containing toothpaste had a superior effect on reducing dentin permeability to fluoride toothpaste.

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