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Effect of antioxidant/reducing agents on the initial and long-term bonding performance of a self-etch adhesive to caries-affected dentin with and without smear layer-deproteinizing

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ABSTRACT

This study aimed to evaluate the effect of a reducing agent containing *p*-toluenesulfinic acid sodium salt (Accel®) and plant-extract antioxidant (rosmarinic acid solution) on the bonding durability of a self-etch adhesive to caries-affected dentin with and without smear layer-deproteinizing with NaOCl solution. The caries-affected dentin were assigned to pretreatment of smear layer-deproteinizing with NaOCl solution or none, then subdivided to reducing agent/antioxidant treatment with *p*-toluenesulfinic acid sodium salt or rosmarinic acid solution or none. After bonding with 2-step self-etch adhesive and restoring with resin composite, the specimens were stored in artificial saliva for 24 h or 1 year. The microtensile bond strength (μTBS) were analyzed by three-way ANOVA with post-hoc Tukey's test and *t*-test ($p < 0.05$). The collagen-fibril status at hybridized complex was observed under TEM. The results showed that μTBS to caries-affected dentin significantly decreased after 1-year of storage ($p < 0.05$). Smear layer-deproteinizing with NaOCl significantly decreased μTBS to caries-affected dentin despite eliminating hybridized smear layer, however a subsequent application with *p*-toluenesulfinic acid sodium salt and rosmarinic acid solution significantly increased initial bond strengths ($p < 0.05$) and maintained the bond strengths after 1-year of storage ($p > 0.05$), with preservation of collagen-fibril integrity within authentic hybrid layer. Therefore, the additional application of *p*-toluenesulfinic acid sodium salt and rosmarinic acid solution after smear layer-deproteinizing with NaOCl could improve initial and long-term bond strengths of a self-etch adhesive to caries-affected dentin.

1. Introduction

Mild self-etch adhesives, especially 10-MDP containing adhesives, are considered to be a gold standard for bonding to dentin [1–3]. They can simultaneously demineralize smear layer-covered dentin surfaces and infiltrate resin monomers, leading to superior initial resin-dentin bond. Also the acidic functional monomers, which form stable chemical bonds to calcium in the dentin substrate, can promote reliable bonding durability to dentin [4–6]. However, these self-etch adhesives cannot completely remove smear layers due to their mild acidity. The remnants of the smear layer on dentin surface can form hybridized smear layer, being encapsulated by adhesive resin, and the underlying demineralized dentin can form authentic hybrid layer with impregnation with adhesive resin [7]. The presence of smear layer was reported to hamper monomer penetration into the underlying dentin, and compromise initial bonding performance to dentin [8,9]. Additionally, the incomplete monomer penetration into dentin causes nanoleakage formation within hybrid layer [10,11], which can permit water penetration into the resin-dentin interface, and leads to the hydrolytic degradation of the interface over time [12,13].

Smear layer-deproteinizing with oxidizing agents, such as sodium hypochlorite (NaOCl) or hypochlorous acid (HOCl) solution, has been

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introduced as a pre-treatment method for improvement of dentin bonding with self-etch adhesives [14–16]. This technique could eliminate the hybridized smear layer and facilitate monomer penetration due to removal of the organic phase of the smear layer [10,15]. However, the longer application time of NaOCl could compromise dentin bond strength [14,17], because the remnants of NaOCl and its by-product could have a negative effect on the polymerization of dental adhesive [18]. The adjunctive application of antioxidant/reducing agents on NaOCl-treated dentin was then studied and found to reverse the compromised bond strength via neutralization of the oxidizing effect [19–22]. The reducing agent Accel® containing *p*-toluenesulfinic acid was demonstrated to have polymerization accelerating activity [23,24] as well as antioxidant activity [21,25]. Rosmarinic acid of plant-extract antioxidant can act as a cross-linker of collagen fibrils and inhibit MMPs [26–28]. The application of Accel® or rosmarinic acid solution can improve the compromised initial bond strength of self-etch adhesives to smear layer-deproteinized dentin with NaOCl solution [21], and has been demonstrated to improve the long-term stability of resin-normal dentin bonding performance for 1-year storage in artificial saliva regardless of NaOCl pre-treatment [22].

Under minimal intervention (MI) concept with preservation of remineralizable tissue by selective removal of caries-infected dentin, bonding substrate is mainly composed of caries-affected dentin, not normal dentin. Many studies have demonstrated that caries-affected dentin decreased initial bonding performance with thicker and more porous hybrid layer [29–32]. Additionally, the bond durability of caries-affected dentin bonded with either etch-and-rinse or self-etch system was less than normal dentin due to its more susceptibility to hydrolytic degradation [29–33]. Unfortunately, there is no definitive evidence to support particular materials being more suitable than others for restoring teeth after selective carious removal [34]. Smear layer-deproteinizing technique with NaOCl is supposed to be more effective on caries-affected dentin than normal dentin with respect to improving initial bond strengths of self-etch adhesives because caries-affected dentin has thicker organic phase-enriched smear layer [14,15,31]. However, porous structure of caries-affected dentin might allow the oxidizing effect by NaOCl treatment to entrap in the deeper region, which might affect the bonding stability. There is limited published information on effects of smear layer-deproteinizing with NaOCl, especially with the following application of antioxidant/reducing agents on the bonding stability to caries-affected dentin.

The purpose of this study was therefore to evaluate the effect of Accel® and rosmarinic acid on the initial and long-term bonding performance of a 2-step self-etch adhesive (Clearfil™ SE Bond) to caries-affected dentin with and without smear layer-deproteinizing with NaOCl solution. The null hypothesis tested was that the application of antioxidant/reducing agents do not improve the initial and long-term microtensile bond strengths of a 2-step self-etch adhesive to caries-affected dentin with and without smear layer-deproteinizing.

2. Materials and methods

2.1. Specimen preparation

One hundred and eighty extracted carious human molars stored frozen were used in this study, according to a protocol approved by Human Research Ethics Committee, Tokyo Medical and Dental University, Tokyo, Japan. The occlusal enamel was ground down under water lubrication perpendicular to the long axis of the tooth to expose a flat surface of middle to deep dentin within the carious lesion. The carious lesion was then evaluated by staining with CARIES DETECTOR (Kuraray Medical, Tokyo, Japan), whereby the dark-red-stained dentin was classified as caries-infected dentin, and the light-pink-stain was classified as caries-affected dentin. A further reduction of the caries-infected dentin was performed by abrasion with 600-grit silicon carbide (SiC) paper under running water to obtain flat surfaces of smear layer-covered caries-affected dentin. The teeth were randomly divided into two groups: with or without NaOCl treatment for 30 s. After rinsing with water for 10 s and air drying, the dentin surfaces were further divided into three sub-groups as follows: no application of antioxidant, application of Accel® (Sun Medical Co., Ltd., Kyoto, Japan) of *p*-toluenesulfinic acid sodium salt solution for 5 s, and application of 100 μM rosmarinic acid in 5% ethanol for 5 s.

After air-drying, a 2-step self-etch adhesive system (Clearfil™ SE Bond, Kuraray Noritake Dental Inc., Tokyo, Japan) was applied to all the dentin surfaces according to the manufacturer's instructions (Table 1), and resin composite (Clearfil® AP-X, Kuraray Noritake Dental Inc., Tokyo, Japan) was built up in three 1.5 mm increments. Each increment was light-cured for 20 s with a light-curing unit (830 mW/cm^2; Optilux 501, Kerr Corporation, CA, USA).

2.2. Microtensile bond strengths (μTBS) test

After water storage at 37 °C for 24 h, the bonded teeth were vertically sectioned into 0.7 mm-thick slabs through the caries-affected portion using a low-speed diamond saw (IsoMet™ Low Speed Saw, Buehler Ltd., Lake Bluff, IL, USA) under water lubrication. The slabs were hand-trimmed to an hour-glass shape, thereby isolating the caries-affected dentin with a cross-sectional area of approximately 0.7 x 1.4 mm^2, using a cylinder-shaped fine diamond bur (Intensive SA, Swiss Dental, Zurich, Switzerland) in a high speed handpiece with water spray. The thickness and width of the bonded interface were measured using a digital micrometer (Digimatic Solar, Mitutoya Crop., Tokyo, Japan). The specimens in each group were randomly divided into two groups for storage in artificial saliva for 24 h or 1 year (fresh artificial saliva was replenished every week). The artificial saliva was prepared in accordance with Pashley et al. [35] without the protease inhibitor. After the designated storage period, all the specimens were subjected to the microtensile bond strength test in a universal testing machine (EZ Test, Shimadzu, Kyoto, Japan) at a cross-head speed of 1 mm/min.

The normality of microtensile bond strength data was tested using the Levene's test, then data were statistically analyzed using three-way ANOVA, and Tukey's test and *t*-test were used as post-hoc tests. All

Table 1
Materials used in the study.

Material	Manufacturer	Batch number	Composition	Bonding procedure
Accel®	Sun Medical Co., Ltd., Kyoto, Japan	MM2F	*p*-toluenesulfinic acid sodium salt, ethanol, water	
Clearfil™ SE Bond	Kuraray Noritake Dental Inc., Tokyo, Japan	01042A	Primer: 10-MDP, HEMA, Hydrophilic aliphatic dimethacrylate, N, N-diethanol-p-toluidine, CQ, Water Bond: bis-GMA, HEMA, DMA, 10-MDP, Toluidine, Silanated silica, CQ	Apply Primer for 20 s; Gently air dry by compressed air spray Apply Bond; Light cure for 10 s
Clearfil® AP-X	Kuraray Noritake Dental Inc., Tokyo, Japan	1016AB	bis-GMA, TEGDMA, Silanated barium glass filler, Silanated silica filler, Silanated colloidal silica, CQ, Initiators, Accelerators, Pigments	

Abbreviations: 10-MDP: 10-Methacryloyloxydecyl dihydrogen phosphate; HEMA: 2-hydroxyethyl methacrylate; CQ: Camphorquinone; bis-GMA: 2,2-bis [4-(2-hydroxy-3-methacryloyloxypropoxy) phenyl]propane; DMA: dimethacrylate; TEGDMA: Triethyleneglycol dimethacrylate.

statistical analyses were performed at a confidence level of 95% using SPSS Ver. 22.0 (SPSS; Chicago, IL, USA).

2.3. Failure mode analysis

After bond strength testing, the dentin sides of the specimens were observed using a stereomicroscope (Nikon SMZ1000, Nikon Corp., Kanagawa, Japan) at 120X magnification for failure mode determination. Failure modes were classified according to one of four types as described by Prasansuttiporn et al. [36]:

Type 1: Mixed failure (mixed with adhesive failure between resin and dentin, and cohesive failure in bonding agent and/or dentin)
Type 2: Adhesive failure (80–100% of the failure occurred between resin and dentin)
Type 3: Cohesive failure in dentin (80–100% of the failure occurred in the underlying dentin)
Type 4: Cohesive failure in resin (80–100% of the failure occurred in the adhesive resin and/or overlying composite)

Failure modes were analyzed for statistically significant differences by the nonparametric Pearson's chi-squared test. All statistical analyses were performed at a confidence level of 95% using SPSS software version 22 (SPSS; Chicago, IL, USA).

2.4. TEM observation

To examine the morphology at the resin-dentin interfaces, two additional teeth in each group which were pre-treated as described above and restored with low-viscosity composite (Protect Liner F; Kuraray Noritake Dental Inc., Tokyo, Japan) were prepared. The 0.9-mm thick hour-glass shaped slabs isolating caries-affected dentin were obtained before storage in artificial saliva for 24 h or 1 year. After designated water storage, the specimens were undergone fixing process and cut into 70-nm thick ultrathin sections. In order to observe collagen status, 1-year aged specimens were undergone demineralization and staining processes with 1% phosphotungstic acid followed by 2% uranyl acetate. The observation was taken under transmission electron microscope (TEM; H-7100, HITACHI, Tokyo, Japan) operating at 75 kV.

3. Results

3.1. μTBS test

The results of microtensile bond strengths are summarized in Table 2. Three-way ANOVA revealed that there were significant differences in smear layer-deproteinizing ($p = 0.009$), antioxidant application ($p < 0.001$), and storage period ($p = 0.001$). There were significant interactions between smear layer-deproteinizing and antioxidant application ($p < 0.001$), and between antioxidant application and storage period ($p = 0.048$), but no interaction between smear layer-deproteinizing and storage period ($p = 0.997$). Tukey's multiple comparisons revealed that for 24-h storage, smear layer-deproteinization significantly reduced the bond strength on caries-affected dentin ($p < 0.05$), while a subsequent application of Accel® and rosmarinic acid significantly increased the bond strengths ($p < 0.05$). *T*-test analysis revealed that 1-year storage significantly decreased bond strengths to caries-affected dentin compared with 24-h storage, regardless of smear layer deproteinization ($p < 0.05$). The Accel® and rosmarinic acid application maintained the bond strengths to caries-affected dentin with and without smear layer-deproteinizing with NaOCl solution ($p > 0.05$).

Table 2
Mean and standard deviation of microtensile bond strengths (MPa) n = 15.

Groups		Storage time	
		24 h	1 year
Caries-affected dentin	No treatment	35.1 (5.3)^{A1}	30.3 (4.2)^{a2}
	Accel®	36.1 (5.6)^{A1}	34.7 (4.7)^{a1}
	Rosmarinic acid	35.4 (5.5)^{A1}	34.2 (4.3)^{a1}
Smear layer-deproteinized caries-affected dentin	No treatment	28.2 (4.3)^{B1}	23.1 (4.5)^{b2}
	Accel®	41.9 (4.8)^{C1}	40.7 (4.4)^{c1}
	Rosmarinic acid	42.1 (4.9)^{C1}	41.1 (4.6)^{c1}

Significant differences in each column were represented by the different superscript letters. Significant differences in each row were represented by the different superscript numbers ($p < 0.05$).

3.2. Failure modes analysis

The failure modes are summarized in Fig. 1. In all the groups, the majority of failure modes were mixed failure. There were no significant differences in failure modes between the experimental groups ($p = 0.054$).

3.3. TEM observation

In 24-h aged specimens of caries-affected dentin, there were no morphological alterations at the interfaces among no-pretreated, Accel®-pretreated, and rosmarinic acid-pretreated groups, in which thick hybridized smear layer (Hs) was loosely aligned on the authentic hybrid layer (Ha). (Fig. 2A, B, C, respectively). Smear layer-deproteinizing with NaOCl eliminated Hs, but the collagen fibrils in Ha were intact, regardless of the following application of Accel® and rosmarinic acid agents (Fig. 2D–F).

For 1-year aged specimens of caries-affected dentin, in the no-pretreated group, collagen fibrils in Ha could not be traced with the presence of disorganized Hs (Fig. 3A). On the other hand, in the Accel®-pretreated and rosmarinic acid-pretreated groups, collagen fibrils in Ha were still intact with some banded collagen fibrils (Fig. 3B and C, respectively). The NaOCl-smear layer deproteinizing group revealed the discontinuous surface at the top of Ha without Hs (Fig. 3D), whereas in the following application of Accel® and rosmarinic acid groups, the evenly intact Ha was observed with tracable collagen fibrils (Fig. 3E and F, respectively).

4. Discussion

The results of this study showed that the application of Accel® and rosmarinic acid were able to maintain the bond strength of a 2-step self-etch adhesive (Clearfil™ SE Bond) to caries-affected dentin for 1-year storage in artificial saliva, regardless of smear layer-deproteinizing with 30-s NaOCl. Smear layer-deproteinizing alone did not improve the bonding performance to caries-affected dentin, whereas a subsequent application with Accel® and rosmarinic acid could improve both initial and long-term bond strengths to caries-affected dentin. Thus, the null hypothesis was partially rejected.

For a resin adhesive-composite restoration, large areas of the cavity floor are composed of caries-affected dentin after removal of caries-infected dentin. Caries-affected dentin is different in morphological, chemical and physical characteristics to normal dentin due to dynamic cycles of demineralization and remineralization occurring with the carious process [37]. That is, caries-affected dentin is partially demineralized, resulting in higher porosity, lower mechanical properties and higher water content in the intertubular region [38], while the dentinal tubules are occluded by mineral deposits [39]. These alterations produce lower bond strengths to caries-affected dentin compared to normal dentin regardless of the type of adhesive system (etch-and-rinse system or self-etch system) [29,31,33]. Additionally, the prepared smear layer

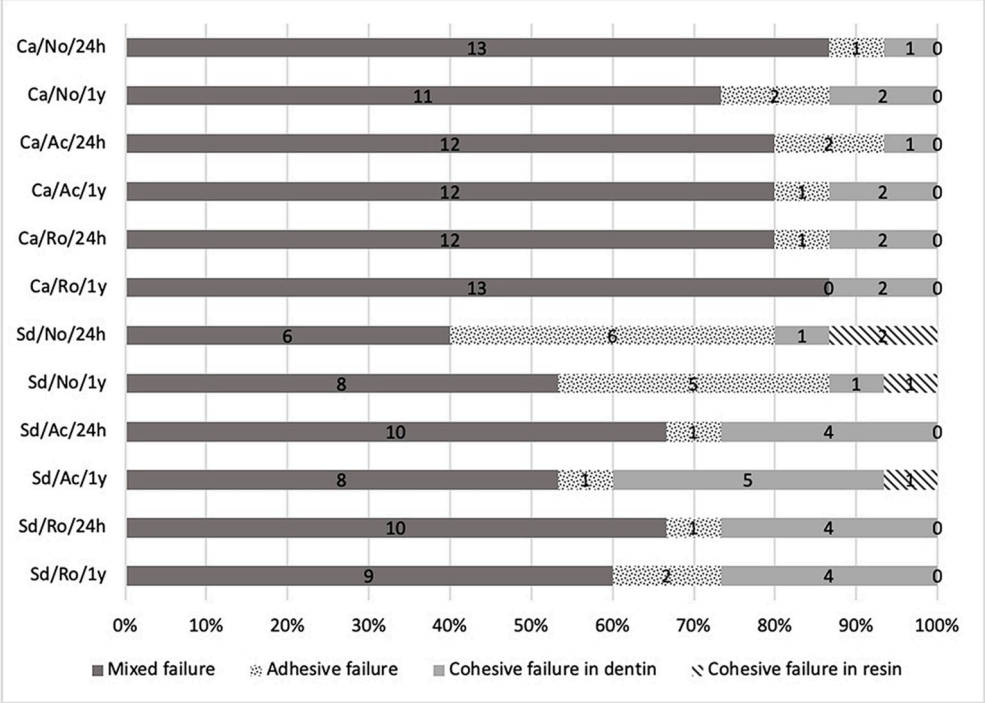

Fig. 1. Failure mode of resin-dentin bond in each group (n = 15). Number in each bar refers to the fractional failure mode in each group.
Abbreviations: Ca: caries-affected dentin; Sd: smear layer-deproteinized caries-affected dentin; No: No treatment; Ac: Accel® treatment; Ro: rosmarinic acid treatment; 24 h: 24-h storage; 1y: 1-year storage.

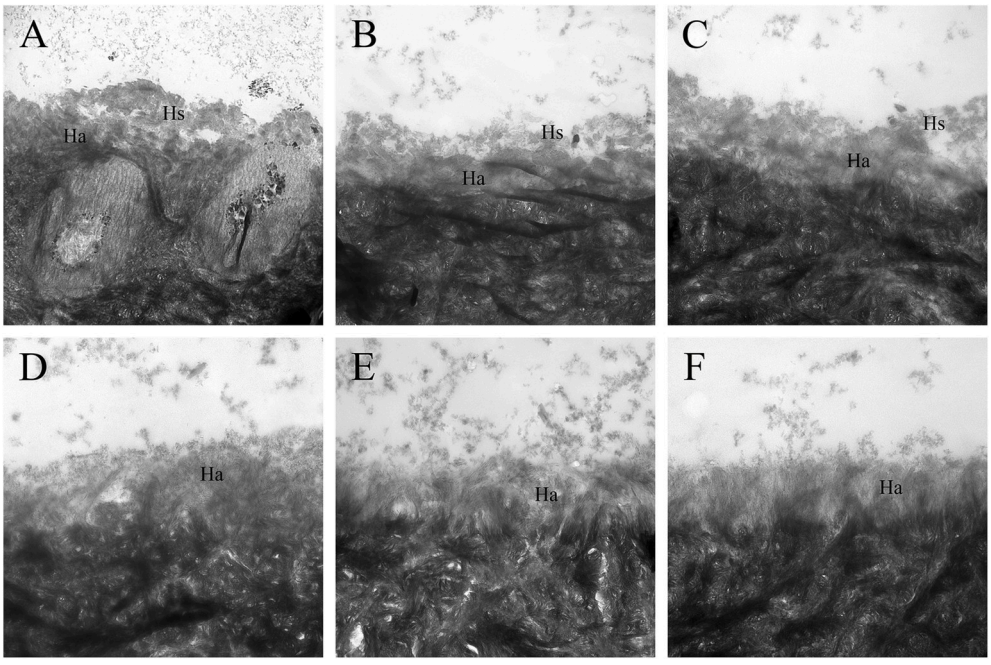

Fig. 2. TEM micrographs of 24-h aged bonded caries-affected dentin. No-pretreated group (A) showed thick hybridized smear layer (Hs) dispersedly located on top of authentic hybrid layer (Ha) (x8000). The Accel® application (B) and rosmarinic acid application (C) prior to bonding procedure did not change the morphology of hybridized complex; Hs were remained, and the collagen fibrils in Ha were intact (x30000). Smear layer-deproteinizing with NaOCl (D), smear layer-deproteinizing with NaOCl followed by Accel® application (E), and smear layer-deproteinizing with NaOCl followed by rosmarinic acid application (F) revealed continuity of Ha from adhesive layer without Hs, and the collagen fibrils in Ha were intact (x30000).

on caries-affected dentin is thicker with an enriched organic phase compared to that of normal dentin, resulting in incomplete monomer penetration into underlying dentin and poor quality of hybrid layer when self-etch adhesives are used [15]. In the present study, it has been demonstrated that the bond strength of resin-caries-affected dentin (without any treatments) decreased over 1-year of storage in artificial saliva, with the degradation of hybrid layer. These could be attributed to the hydrolytic degradation of resin and subsequent enzymatic degradation of exposed collagen fibrils in the hybrid layer. Since caries-affected dentin contains higher quantities of MMP-2, MMP-9, and cysteine cathepsins enzymes than that of normal dentin [40]. With the use of a self-etch adhesives, these enzymes can be activated and aggravate the degradation of exposed collagen fibers [41], which are apparently found at the base of hybrid layer in resin-caries-affected dentin interface [33].

Antioxidant/reducing agents used in this study were Accel® and rosmarinic acid. Accel® containing *p*-toluenesulfinic acid salt has been introduced as an agent for improving the bond strength to NaOCl-

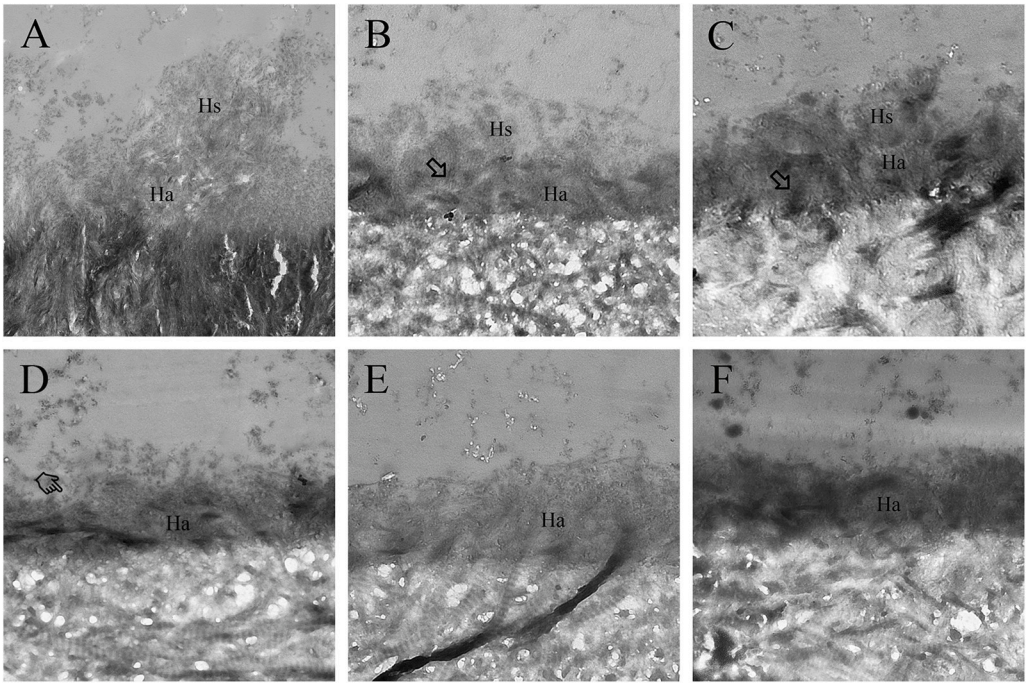

Fig. 3. TEM micrographs of 1-year aged bonded caries-affected dentin (x30000). No-pretreated group (A) showed deterioration in both hybridized smear layer (Hs) and authentic hybrid layer (Ha) as collagen fibrils could not be obviously observed. The Accel®-(B) and rosmarinic acid-(C) pretreated groups exhibited intact Ha with some banded collagen fibrils (arrows). In the NaOCl-smear layer deproteinizing group (D), the intermittent collagen strands were observed at the surface of Ha (pointer). Smear layer-deproteinizing with NaOCl followed by Accel® application (E) and smear layer-deproteinizing with NaOCl followed by rosmarinic acid application (F) revealed evenly intact Ha with evidence of intact collagen fibrils.

treated dentin [42] or used as a pretreatment agent for adhesive root canal sealer after endodontic irrigation with NaOCl solution to reduce the oxidative effect [25]. Rosmarinic acid is a plant-extract antioxidant composing of diphenolic compound (a-o-caffeoyl-3, 4-dihydroxyphenyl-lactic acid), which has the ability to control free radical oxidation from its four phenolic hydrogens (-OH) [43,44]. The –OH group of phenol can scavenge reactive radicals by causing the electron delocalization into the aromatic ring. As a result, the reactive radicals become poorly reactive with limited reactivity [45]. Apart from antioxidant/reducing property of these agents, salt of *p*-toluenesulfinic acid contained in Accel® is an effective accelerator for the polymerization of methyl methacrylate [46]. It can interact with acidic monomer and generate free radical for initiating radical polymerization [24]. Its presence can increase the degree of conversion of the resin adhesive [47]. On the other hand, rosmarinic acid possesses cross-linking and MMP-inhibition abilities. Its cross-linking effect belongs to the interaction with proline-rich proteins such as collagen [28], enhancing the resistance of collagen to proteolytic degradation, whereas its MMP-inhibitory effect was proved on MMP-9 activity, resulting in the decreased enzymatic degradation of collagen [27].

In present study, the application of Accel® and rosmarinic acid was able to maintain the bond strength, as well as the integrity of collagen in authentic hybrid layers of a 2-step self-etch adhesive bonded to caries-affected dentin over 1-year storage in artificial saliva. These results are in agreement with the previous study on bonding to normal dentin [22]. It was speculated that the ethanol solvent in Accel® could further remove dentinal water upon solvent evaporation [48], whereas the Accel® itself might increase the degree of conversion of the resin adhesive. Thus, the susceptibility of the polymerized adhesive to resin hydrolysis was reduced [49]. On the other hand, the cross-linking and MMP-inhibition abilities of rosmarinic acid contributed to an increased hydrolytic resistance of collagen, and the bonding stability to caries-affected dentin could be obtained.

Previously, smear layer-deproteinizing with oxidizing agents (NaOCl and HOCl solutions) was reported to improve the bond strengths of self-etch adhesives to caries-affected dentin by thinning of the smear layer and eliminating of the hybridized smear layer [14,16]. The mechanism is explained by the chlorination of protein, which is then broken down into radicals and induces the fragmentation of organic phase in smear layer [50]. Therefore, NaOCl treatment can facilitate monomer penetration in self-etch adhesive system [10]. However, the effect of NaOCl pre-treatment on bonding of self-etch adhesive to caries-affected dentin would be time- and concentration-dependent [51,52]. The previous study demonstrated that 15-s pre-treatment of 6% NaOCl could improve the microtensile bond strength of a self-etch adhesive to caries-affected dentin, but not a 30-s pre-treatment of 6% NaOCl [14]. These would be because extending the application time of NaOCl could increase the remnants of NaOCl and its by-products on dentin surface. The remaining oxidizing effect of NaOCl produces premature chain termination and incomplete polymerization of the resin adhesive, since the generated free radicals can compete with the propagating vinyl free-radicals of the resin adhesive [53]. Therefore, the simple treatment of NaOCl for 30 s on caries-affected dentin decreased the bond strength due to suboptimal polymerization of resin adhesive, despite the elimination of hybridized smear layer. Furthermore, the bond strength of NaOCl-treated caries-affected dentin decreased following 1-year storage in artificial saliva, because suboptimal polymerized adhesive was susceptible to resin hydrolysis and subsequently exposed collagen degradation could be occurred.

In this study, the initial bond strengths to caries-affected dentin could be improved by the additional application of Accel® and rosmarinic acid after NaOCl-treatment for 30 s. Accordingly, a subsequent application of antioxidant/reducing agents to neutralize the remaining oxidizing effect of NaOCl and restore the compromised bond strengths to NaOCl-oxidized dentin has been studied [20–22,42]. According to Raman analysis, Accel® could increase the degree of conversion of adhesive bonded on NaOCl-treated dentin [54]. Therefore, the 30-s pre-treatment of NaOCl could eliminate the hybridized smear layer and facilitate monomer penetration due to removal of organic phase of the thick smear layer on caries-affected dentin and the subsequent application of Accel® and rosmarinic acid could obtain optimal polymerization of resin adhesive due to neutralization of the remaining oxidizing effect of NaOCl.

For 1-year storage in artificial saliva, the additional application of Accel® and rosmarinic acid could maintain bond strengths of the self-etch adhesive to caries-affected dentin with NaOCl-smear layer-deproteinizing. These results are in agreement with the previous study using normal dentin with NaOCl-smear layer-deproteinizing [22]. Moreover,

the preserved collagen strands in authentic hybrid layers observed in this study indicated either the resin or collagen resistance to hydrolysis. It was speculated that the Accel® and rosmarinic acid left after redox reaction with oxidized by-products of NaOCl would act as polymerization accelerator and crosslinker/MMP-inhibitor, respectively.

If the reducing components of Accel® and rosmarinic acid were completely consumed due to its redox reaction with oxidized by-products of NaOCl, then the synergistic effect of the elimination of hybridized smear layer and enhancement of monomer penetration by smear layer-deproteinizing might play a more significant role for dentin bonding stability. Further research is required on effect of smear layer-deproteinizing on the dentin bonding stability of self-etch adhesives, excluding the using of antioxidant/reducing agents. Other protocols to eliminate the oxidizing effect such as scrubbing technique [36] or using alternative smear layer-deproteinizing agent such as a mild acidic HOCl solution [10] would be of interest if the smear layer-deprotienizing protocol and/or adhesive application technique can be adjusted to give time- and cost-effective results using the other self-etch adhesives.

5. Conclusion

Within the limitations of this study, it was concluded that the application of Accel® and rosmarinic acid could maintain the microtensile bond strength of a self-etch adhesive to caries-affected dentin over time. Furthermore, they could improve both the initial and long-term bond strengths of the self-etch adhesive to caries-affected dentin with NaOCl-smear layer-deproteinizing. The NaOCl-smear layer deproteinizing with following application of antioxidant/reducing agents could be suitable methods for restoring teeth with self-etch adhesives after selective carious removal albeit the increase in bonding steps.

Declaration of competing interest

None.

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