Polydopamine-Induced Tooth Remineralization

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ABSTRACT: Inspired by mussel bioadhesion in nature, dopamine is extensively used for biomaterial surface modification. In this study, we coated dopamine on demineralized enamel and dentin surfaces to evaluate the effect of polydopamine coating on dental remineralization. Dental slices containing enamel and dentin were first etched with 37% phosphoric acid for 2 min, followed by immersion in a 2 mg/mL freshly prepared solution of dopamine (10 mM Tris buffer, pH 8.5) for approximately 24 h at room temperature in the dark to obtain polydopamine coating. Then, the dental slices with and without polydopamine coating were immersed in the supersaturated solution of calcium and phosphate at 37 °C for 2 and 7 days. The supersaturated solution of calcium and phosphate was refreshed each day. The precipitates were characterized by SEM, XRD, FTIR, microhardness, and nanoscratch analyses. No significant difference was observed in the remineralization of enamel whether it was coated with polydopamine or not. However, a significant difference was found in dentin remineralization between dentin with and without polydopamine coating. Polydopamine coating remarkably promoted demineralized dentin remineralization, and all dentin tubules were occluded by densely packed hydroxyapatite crystals. Thus, coating polydopamine on dental tissue surface may be a simple universal technique to induce enamel and dentin remineralization simultaneously.

KEYWORDS: mussel-adhesion, polydopamine, enamel, dentin, remineralization, hydroxyapatite
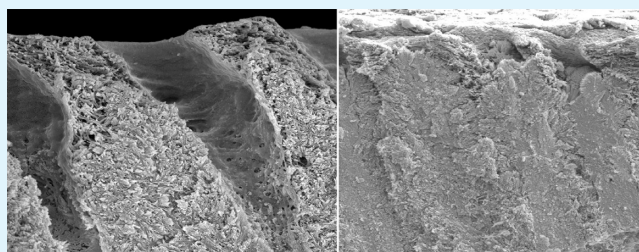
1. INTRODUCTION

Remineralization of the superficial dental tissue, as a non-invasive therapeutic technique in clinical dentistry, has received increased attention, and its therapeutic importance has been generally accepted in recent decades.[1,2] Except for supersaturated solutions of calcium, phosphate, and fluoride as common agents used for remineralization in clinical dentistry, new remineralization techniques have been developed and have been in much greater demand.[2-4] A casein phosphopeptide-stabilized amorphous calcium phosphate (CPP-ACP or Recaldent), an unstabilized amorphous calcium phosphate (ACP or Enamelon), and a bioactive glass containing calcium sodium phosphosilicate (NovaMin) are three current commercially available remineralization systems. Recently, amelogenin (the major enamel protein composed of approximately 90% of the entire organic matrix) is also used for remineralization study.[5,6] All of the above remineralization systems are effective for remineralizing enamel, even forming enamel prism-like tissue. However, they are all ineffective in remineralizing fully demineralized dentin.

Enamel is the most highly mineralized tissue constituted of approximately 97% mineral, 1% organic material, and 2% water. The basic microstructure of the enamel is composed of nanosized fibril-like carbonate hydroxyapatite (HA) crystals that are tightly packed together to form prisms. The unique prism structures run approximately perpendicular from the enamel-dentin junction toward the tooth surface. On the other hand, dentin, which is less mineralized, is composed of 70% HA minerals, 20% organic matrix (mainly collagen), and 10% water. The dentin is permeated by dentinal tubules, which radiate from the pulp cavity toward the enamel−dentin junction. The tubules are surrounded by dense peritubular dentin composed of mineralized collagen fibrils.[7] Thus, acid-etching enamel results in exposing fresh nano-HA crystals. On the contrary, dentin demineralization results in collagen matrix exposure (Figure 1). Therefore, the mechanisms by which the enamel and dentin remineralize are different. In the presence of apatite seed crystallites, enamel remineralization is a process of epitaxial growth of HA crystals over existing seed crystallites. Such growth is a heterogeneous nucleation thermodynamically more favorable than homogeneous nucleation within a completely demineralized collagen matrix.[2,8,9] Although the role of the collagen matrix during apatite mineralization remains a topic of debate, more evidence supports the notion that the dentinal collagen matrix is ineffective in initializing HA nucleation and growth during in vitro biomimetic mineralization.[8-10] In the present study, we intend to establish a system to remineralize enamel as well as dentin.

Mussels can attach to various surfaces in aqueous conditions, ranging from natural inorganic materials and organic materials to synthetic materials. Such adhesive properties rely on the exhaustively repeated 3,4-dihydroxy-L-phenylalanine (DOPA)
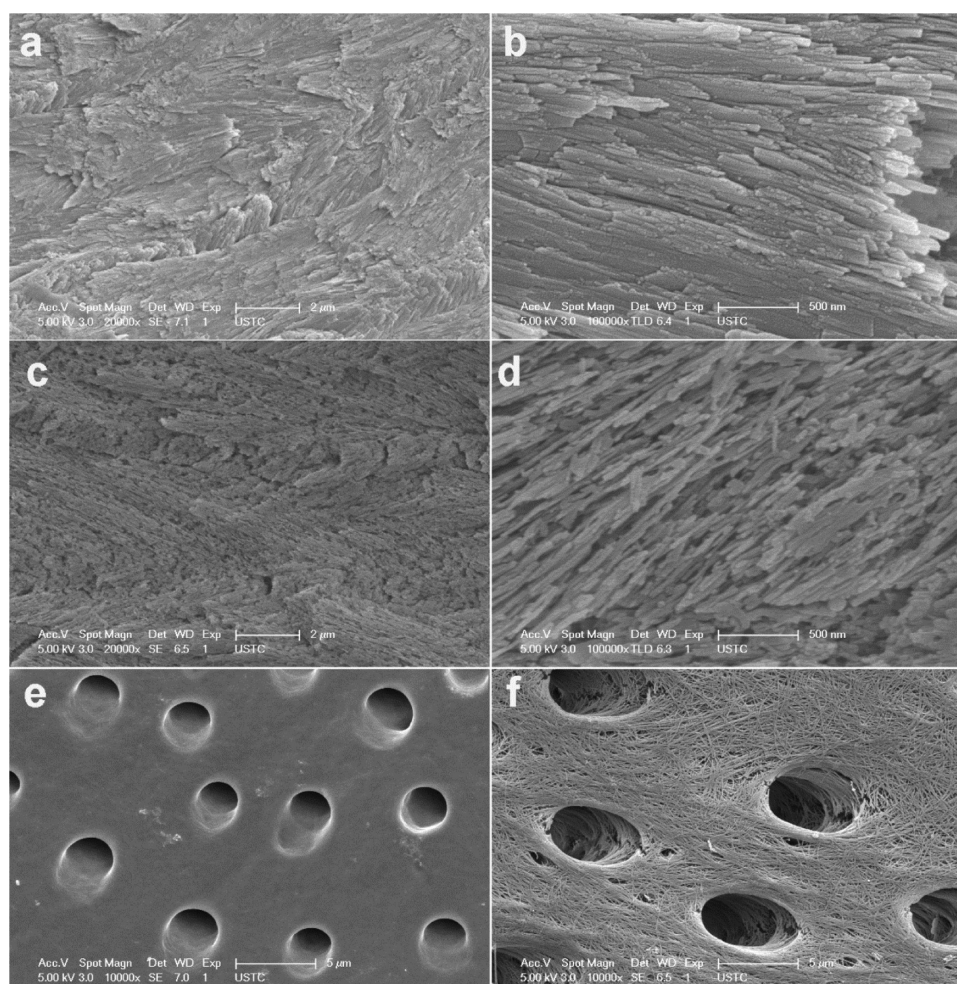
Figure 1. SEM micrographs show enamel and dentin structures before and after etching with 37% H_3PO_4 for 2 min. Panels a and b show the enamel before etching, and panel b is the magnified view of panel a. Panels c and d show the enamel after etching, and panel d is the magnified view of panel c. Panel e shows the dentin prior to etching. Panel f is the dentin after etching, showing the demineralized collagen fiber matrix.

motif in its adhesive foot protein Mefp-5 (*Mytilus edulisfoot protein 5*) secreted by mussels.[11−13] Inspired by this mussel-adhesion phenomenon in nature, dopamine has been extensively used for biomaterial surface modification. The oxidative polymerization of dopamine in aqueous solutions spontaneously forms polydopamine, mimicking DOPA, which exhibits a strong adhesive property to various substrates under wet conditions.[11,14,15] Recently, a method of polydopamine-assisted hydroxyapatite formation (pHAF) has been reported. According to the report, material surfaces activated by polydopamine coating and surface-anchored catecholamine moieties of the polydopamine bound to Ca^{2+} enriches the interface with calcium ions, facilitating the formation of HA crystals that are aligned to the c-axes, parallel to the polydopamine layer. pHAF is a powerful approach in creating HA-based, novel organic−inorganic hybrid biomaterials regardless of type, size, and shape of hybridized counterpart materials.[16,17] Herein, we coated dopamine on demineralized enamel and dentin surfaces with the hypothesis that dopamine coating can induce remineralization of dentin as well as enamel with no side-effects on enamel remineralization.

2. MATERIALS AND METHODS

2.1. Tooth Slice Preparation. Human molars without fillings were selected following the standard procedures for extraction at the Stomatologic Hospital of Anhui Medical University. The necessary informed consent was obtained from the patients. The teeth were treated with 3% sodium hypochlorite to remove bacteria and rinsed with phosphate buffered saline. Tooth crown containing enamel and dentin were cut perpendicular to the longitudinal axis of each tooth using a low speed IsoMet diamond saw (Buehler, Lake Bluff, IL) cooled by water to form 0.5 mm to 1 mm thick, flat slices with a diameter of approximately 8−10 mm. The dental slice surface was mirror-polished using 600 mesh to 3000 mesh sandpapers, and then the dental specimens were cleaned ultrasonically in a detergent solution, acetone, ethanol, and deionized water in turn. The specimens were then dried at room temperature and placed in a polyethylene tube prior to use. A total of 12 dental slices were prepared.

2.2. Preparation of Polydopamine Coating on Acid-Etched Tooth Slices. The dental slices were acid-etched with 37% phosphoric acid for 2 min and rinsed with sufficient deionized water. Then, the acid-etched dental slices without drying were immersed in a 2 mg/mL freshly prepared solution of dopamine (Sigma-Aldrich, St. Louis, MO) (10 mM Tris buffer, pH 8.5) at room temperature in the dark. After 24 h, the substrates were sonicated for 10 min in water thrice to remove the nonattached dopamine and dried under nitrogen.
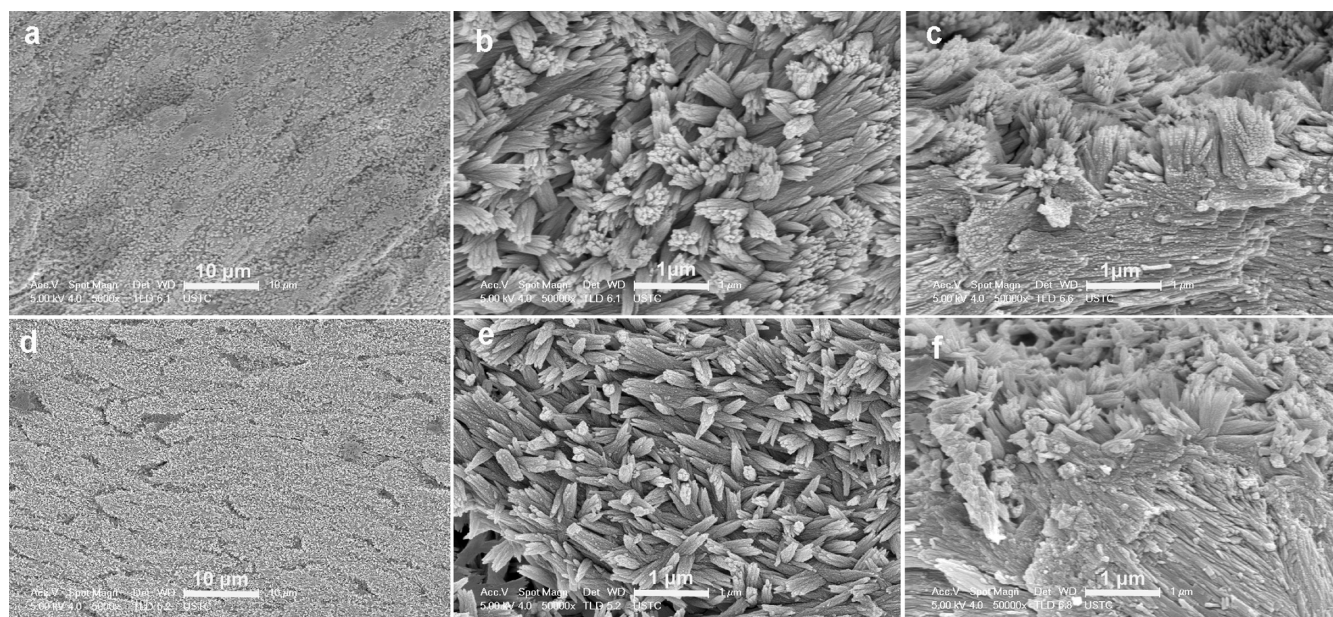
Figure 2. SEM micrographs of crystals that precipitated on the polydopamine-coated enamel surface (a, b, c) or that without polydopamine coating (d, e, f) after mineralization for 2 days. Panels b and e are the magnified views of panels a and d, respectively. Panels c and f are the transverse sections of panels a and d, respectively.

2.3. Remineralization of Dental Tissue Coating Using Polydopamine.
The calcification solution was prepared according to the procedure described by Fan.[5] The solution contained 2.58 mM calcium ($CaCl_2 \cdot 2H_2O$), 1.55 M phosphate (KH_2PO_4), 1 mg/L fluoride (NaF), and 180 mM NaCl and was buffered by 50 mM of trihydroxymethylaminomethane (Tris)-hydrochloric acid. The calcification solution pH was adjusted using 0.1 M HCl and 0.1 M NaOH to 7.6. The solution was stored at 4 °C prior to use.

Dental slices with polydopamine coating (experimental group, $n = 4$) and without polydopamine coating (control group, $n = 4$) were respectively placed at the bottom of sealed polyethylene tubes filled with 10 mL of calcification solution. Then, the polyethylene tubes were continuously stirred at 100 rpm in a shaking incubator at 37 °C. The calcification solution was replaced every day. The tooth slices were removed after 2 and 7 days, cleaned using mild ultrasonication in deionized water, rinsed with running deionized water, and gradually dehydrated to a critical drying point prior to characterization.

2.4. Characterization of the Precipitates of Remineralization.
All the samples were first examined by XRD and FTIR spectroscopy and then by SEM. A typical sample from each group was selected for the microhardness and nanoscratch tests.

The morphology of the precipitates was evaluated by field emission SEM, and the composites were evaluated by XRD (X'Pert Pro, Philips Almelo, Netherlands) and diffuse-reflection FTIR (DR-FTIR) (Nicolet 8700 Thermo Scientific Instrument Co., Friars Drive Hudson, New Hampshire, U.S.A.).

To evaluate the Knoop microhardness of the precipitates on the enamel and the dentin after remineralization for 7 days, one typical sample from the experimental group and the control group was selected using a hardness tester (E. Leitz GmbH., Wetzlar, Germany). A load force of 50 g was used at a hold time of 10 s. The indenter was located with their long axis perpendicular to the surface of the dental slices. Six indentations were performed on the sample, and the mean

values were statistically analyzed by one-way analysis of variance (ANOVA) and Tukey's test at 5% level of significance.

The nanoscratch technique was used to evaluate the binding strength of the precipitate to the substrate. Two-day-old remineralized samples were tested (one typical sample from the experimental group and one from the control group) using a nanoscratch tester (NST) (CSM Corp., Switzerland), and four scratch lines were observed in each sample. A spherical Brinell diamond tip with a radius of 2 μm was used for all the tests. Ramp-load tests were performed, in which the tip was driven through a distance of 200 μm at a velocity of 200 μm/min while the normal load was increased continuously from 0.1 mN to 10 mN or 0.1 mN to 50 mN at a rate of 9.9 or 49.9 mN/s, respectively. The curve of frictional force versus load force was plotted. The point at which frictional force dramatically changed indicated that the coating was scratched broken, which may indirectly suggest the binding strength of the coatings to the substrate, that is to say, the remineralization precipitate binding to the enamel.

3. RESULTS AND DISCUSSION

3.1. SEM Analysis of the Precipitate on the Enamel and Dentin Surfaces.
3.1.1. Precipitates on the Enamel Surface. Crystals uniformly precipitated on the pre-existing enamel crystals in the 2 d old remineralized samples whether the enamel surface was coated with polydopamine or not. The enamel prism outline could be found vaguely (Figure 2a and d). The crystal precipitate nucleated from a specific position on the pre-existing enamel HA crystals, bound well to the enamel HA crystals, and grew in an orientation perpendicular to the enamel surface (Figure 2b, c, e, and f). The crystal precipitate clusters of the polydopamine-coated samples much more easily bundled together in parallel and dense packing to form larger crystals compared with the samples without polydopamine coating (Figures 2b and 2e).

All of the 7 day old remineralized samples were covered by a layer of precipitate, and the enamel structure could not be
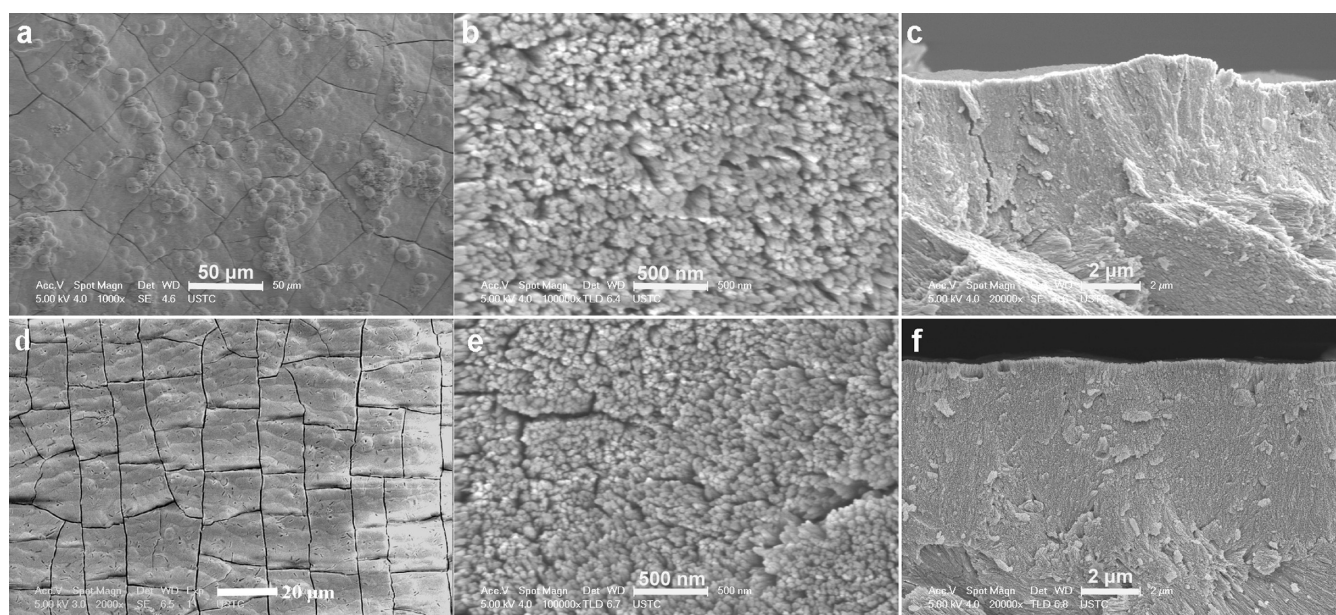
Figure 3. SEM micrographs of the crystals that precipitated on the enamel surface with polydopamine coating (a, b, c) or without polydopamine coating (d, e, f) after remineralization for 7 days. Panels b and e are the magnified views of panels a and d, respectively. Panels c and f show the transverse section of a and d, respectively.
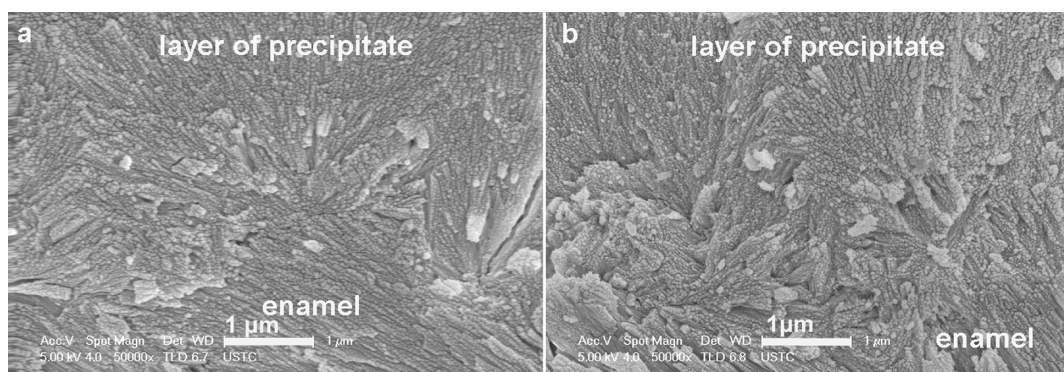

Figure 4. SEM micrographs of the transverse section of the interface between the layer of precipitates and the enamel substrate coated with polydopamine (a) and without polydopamine (b) after mineralization for 7 days.

found (Figure 3a and d). Oriented crystals grew evenly on the enamel surface on the crystallographic *c*-axis perpendicular to the enamel surface (Figure 3b, c, e, and f). In the transverse section, the homogeneous crystals were found oriented in parallel and packed together to form a dense, uniform layer (Figure 3c and f). As the crystals on the surface finally mineralized, the mature state of the underlying area was not reached, and some spaces remained (Figure 3b and e). This result is similar to that reported by Busch.[18] Matured, enamel HA crystals bundled in parallel to form a special microstructure of repeating units of prisms. Thus, we confirmed that the structure of the precipitate was similar to the microstructure of enamel (Figure 1). The interface between the layer of precipitates and the enamel substrate connected very well, showing a tight junction (Figure 4). Figures 2b, c, e, and f, and 4 show that the crystal precipitate directly nucleated and grew on the already existing enamel apatite crystals. Thus, we confirmed that the binding was reliable. The thickness of the precipitate in all the samples was almost equal based on the images of the transverse section, which implied that the rate of precipitation was nearly identical between the two groups.

3.1.2. Precipitates on the Dentin Surface. SEM images showed that polydopamine was successfully coated on the collagen fibers of dentin. Polydopamine bound to collagen fiber very well in particles and filmlike form (Figure 5). In the polydopamine-coated dentin samples after remineralization for 2 days, the dispersed HA crystals deposited on the dentin surface and abundant crystals precipitated in the dentin tubules (Figure 6a−d), but the precipitates were less than that on the enamel (Figure 2). On the contrary, for the dentin samples without polydopamine coating after mineralization for 2 days, few crystal precipitates were found on the dentin surface and in the dentin tubules (Figure 6e−h).

After remineralization for 7 days, all the dentin tubules in the polydopamine-coated dentin samples were occluded by well-defined crystals, and some crystals formed on the dentin surface (Figure 7a, c, and d). However, minimal crystal precipitates were found on the dentin surface and in the dentin tubules of the samples without polydopamine coating (Figure.7b).

3.2. XRD and FTIR Characterization of the Precipitates. In the XRD spectra of all the samples (Figure 8), the diffraction peaks from (002), (211), (112), and (300) planes
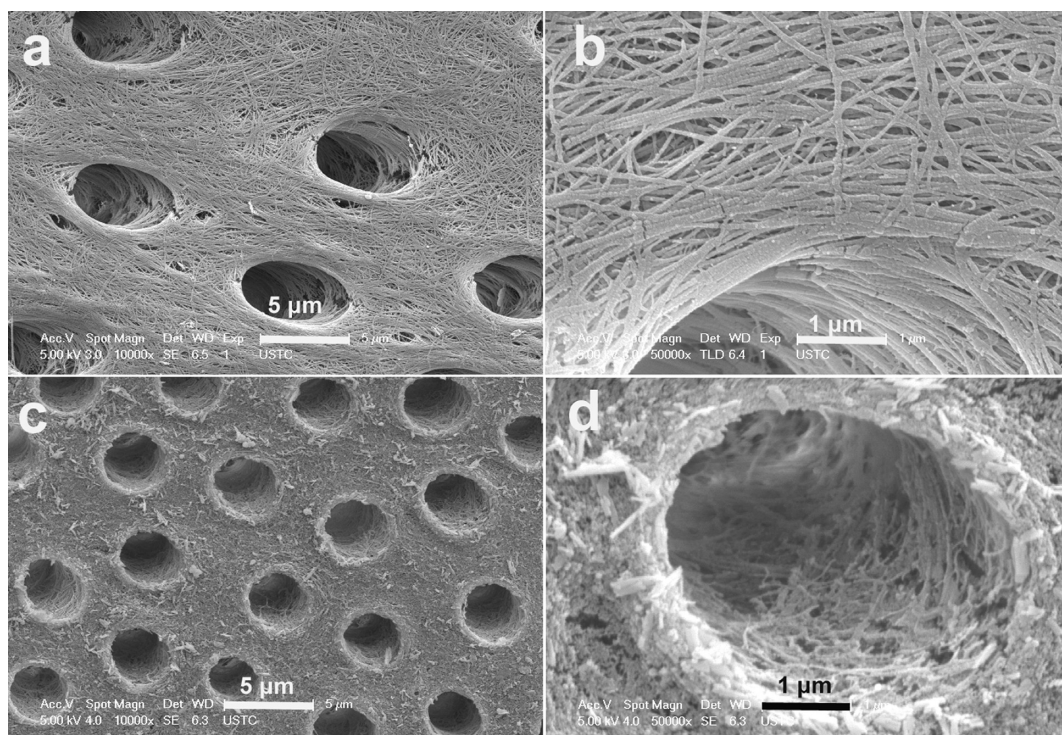
Figure 5. SEM micrographs of acid-demineralized dentin collagens before (a, b) and after (c, d) polydopamine coating. Panels b and d are the magnified views of panels a and c, respectively.

corresponded well to the expected peaks for HA. The ratio of diffraction intensity of the *c*-axis (002) reflection to the diffraction intensity of the (211) or *a*-axis (300) reflections were much more enhanced in the polydopamine-coated sample than those of etched tooth surface and no polydopamine coating. This finding suggests that the HA precipitate was oriented along its *c*-axis. A distinct $-PO_4$ absorption in the FTIR spectra of the precipitate samples with or without polydopamine coating showed remarkable P−O asymmetric stretching ν_3 that belonged to 1027 (ν_{3-1}) and 1120 (ν_{3-2}) cm^{-1}, and P−O bending ν_4 was at 614 (ν_{4-1}) and 571 (ν_{4-2}) cm^{-1}. In the acid-etched dental slice substrate coated with polydopamine, the distinctive peaks attributed to collagen protein and polydopamine were much more remarkable. The peaks at 1624 and 1530 cm^{-1} were attributed to amide I and amide II, respectively, and the peak at 3400 cm^{-1} was attributed to $-NH_3$ or −OH, which was produced from the exposed collagen fiber from acid etching. Taking into consideration the XRD and FTIR spectra, we conclude that the deposit was HA crystals.

3.3. Characterizing the Hardness of the Precipitates and Binding Strength of Precipitates to the Substrate. The hardness of the enamel before and after acid-etching and the precipitates on the enamels were evaluated using Knoop microhardness. Considering that the thickness of the HA precipitate was so thin in the 2 day old remineralized samples that the results would be interfered by the enamel substrate and could not present the real hardness of the precipitate layer. Thus, we selected the 7 day old remineralized samples for the microhardness test (Figure 9). The statistical results of ANOVA showed that the hardness of the enamel before and after acid-etching and the precipitates on all the samples were significantly different. The hardness before and after reminer- alization were likewise significantly different. The statistical

results of Tukey's test showed that acid-etching remarkably reduced enamel hardness (277 ± 19 vs 136 ± 25, $p < 0.05$), and remineralization increased the acid-etched enamel hard- ness, whether it was polydopamine-coated or not (136 ± 25 vs 186 ± 51 or 182 ± 47, $p < 0.05$). However, the remineralization did not reach the hardness of the untreated enamel ($p < 0.05$), and no significant difference in hardness was found between the remineralized groups whether polydopamine-coated or not (186 ± 51 vs 182 ± 47, $p > 0.05$).

Figure 10 shows the hardness changes in dentin before and after remineralization for 7 days (Figure 10). The ANOVA results showed that the hardness of dentin before acid-etching was significantly different from the acid-etched dentin and the precipitates. Tukey's test showed that acid-etching remarkably reduced dentin hardness (58.7 ± 6.0 vs 44.7 ± 9.3, $p < 0.05$). Remineralization increased the hardness of the acid-etched dentin with polydopamine coating (50.7 ± 10.1 vs 44.7 ± 9.3, $p < 0.05$), but it did not reach the hardness of the untreated dentin. The remineralization did not increase the hardness of the acid-etched dentin without polydopamine coating (44.8 ± 7.4 vs 44.7 ± 9.3, $p > 0.05$).

Nanoscratch measurements were performed to evaluate the binding strength of the HA crystals to the enamel substrate. Considering that the thickness of the HA precipitate was so thick in the 7 d old remineralized samples that the scratch could not penetrate through the HA precipitate layer, we selected the 2 d old remineralized samples for the nanoscratch test. Figure 11 shows the curve of frictional force versus load force and the SEM images of the scratches. At the light load force of 0 mN to 10 mN, the frictional force was increased continuously with the load force increase, and the curve shape was similar between the groups that used polydopamine coating and those that did not (Figure 11, left). The maximum depth of the scratch was approximately 200 nm. The combination of the SEM images of
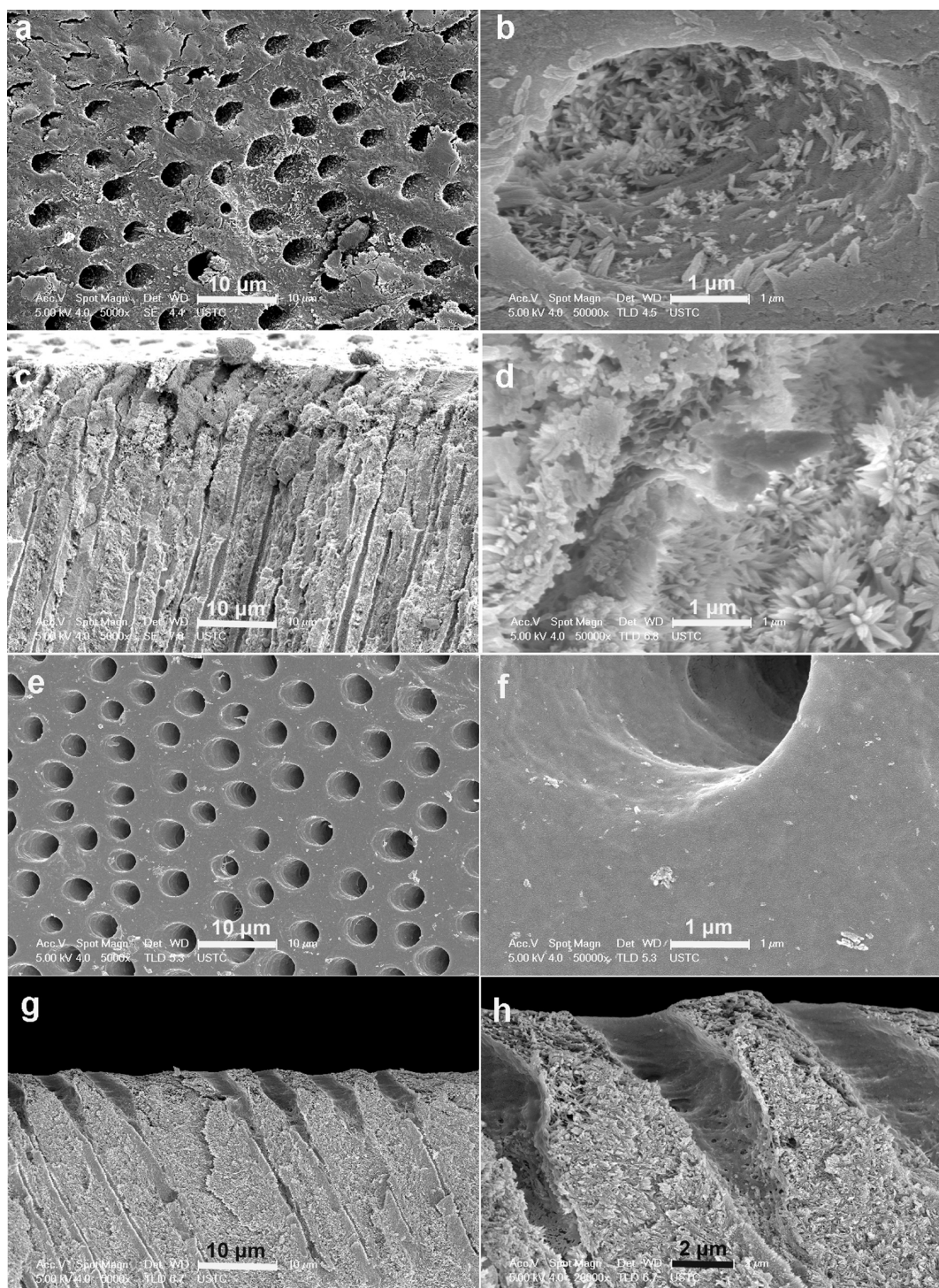
Figure 6. SEM micrographs of the remineralization of the dentin surface coated with polydopamine (a−d) or not (e−h) after mineralization for 2 days. (a and e) View from the surface. (b and f) Magnified views of panels a and e showing the precipitates in the dentin tubule. (c and g) Transverse section view. (d and h) Magnified views of panels c and g, respectively.

the transverse section of the precipitate (Figure.2) and scratch morphology (Figure 11, bottom left) confirmed that the nanoscratch was within the precipitate layer. All the results suggested that the precipitates between the two groups had similar tribological and wear behaviors. However, the heavy load force of 0 mN to 50 mN on the precipitate layer resulted in the continuous increase in frictional force with the load force increase. However, at a certain point, the frictional force dramatically changed (Figure 11, right). The maximum depth

of the scratch extended close to 2000 nm. The combination of the SEM images of the transverse section of the precipitate (Figure.2) and the scratch morphology (Figure 11, bottom right) confirmed that the nanoscratch penetrated the enamel substrate. The critical point for the polydopamine-coated sample was at about the 24 mN mean load force, whereas, samples without polydopamine coating was at about the 26 mN mean load force. No significant difference between the two groups was found about the critical point. The critical point
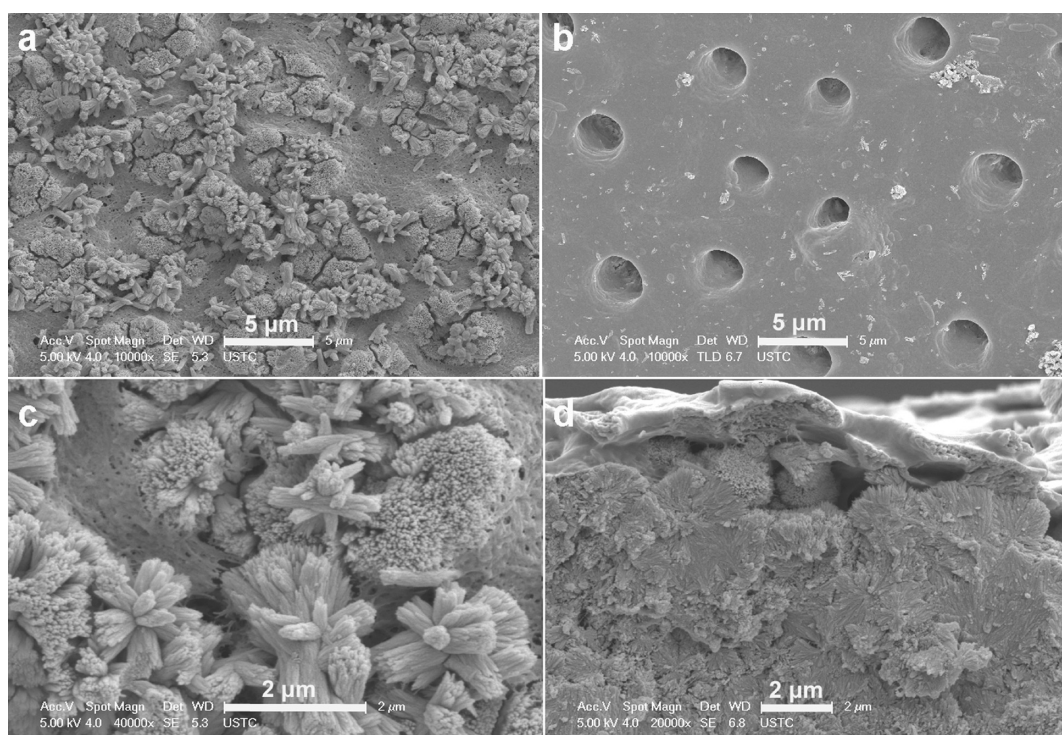
Figure 7. SEM micrographs of dentin surface remineralization with polydopamine coating (a, c, d) or without (b) after remineralization for 7 days. (a and b) View from the surface. (c) Magnified view of panel a showing precipitate crystal growth in dentin tubules. (d) Transverse section view of panel a showing precipitate crystal growth in the dentin tubules.
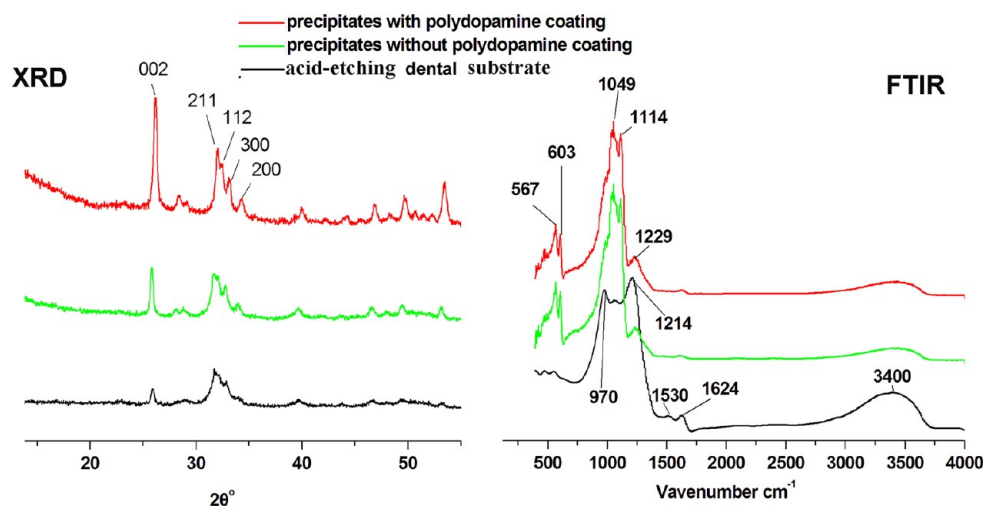

Figure 8. XRD and FTIR spectra of the sample surfaces of 37% H_3PO_4-etched dental slices and precipitates on the dental surface with or without polydopamine coating after remineralization for 2 days.

indicates that the precipitate layer was scratched broken, which may indirectly suggest the binding strength of the precipitate to substrate, that is to say, the remineralization precipitates binding to enamels. Thus, by combining the SEM images of the transverse section of the precipitate (Figure.2) and the scratch morphology (Figure.11), the nanoscratch results implied that precipitate layer has the same binding strength between the groups whether polydopamine coating was used or not.

In our primary experiment, we also intended to apply the nanoscratch test on the remineralized dentin-etched surface, but the results were very confusing and no consistent regularity was found. This phenomenon may have occurred from the demineralized collagen fibrils that were not remineralized and

the precipitates that were distributed unevenly. Minimal HA precipitates were distributed unevenly on the dentin surface in the control group, whereas the HA precipitates were mainly distributed in the dentin tubules in the experimental group. Thus, we finally discontinued the test on dentin surface. However, based on the SEM results, we found that HA crystals nucleated and grew more preferentially in the dentin tubules. The mechanism of the precipitation of the HA crystals in the dentin tubule involves the nucleation, growth, and maturity of the HA crystals rather than the adsorption of existing HA crystals that may have fallen into the dentin tubule. Thus, the binding of the precipitate HA to the dentin tubule was persistent.
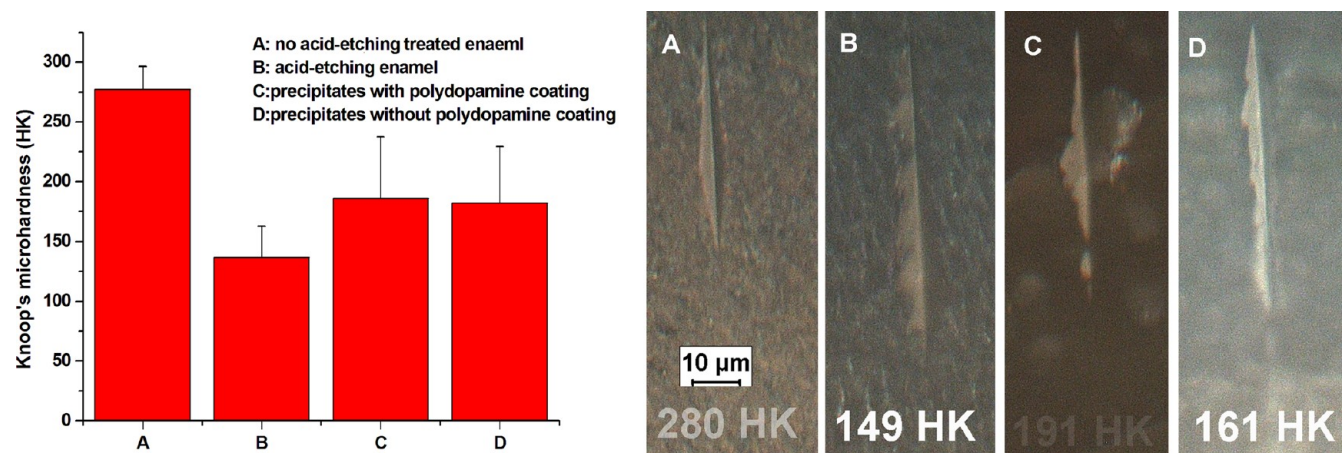
Figure 9. Knoop hardness of the enamel before and after acid-etching and acid-etched enamel after remineralization. The images were the typical indentation marks.
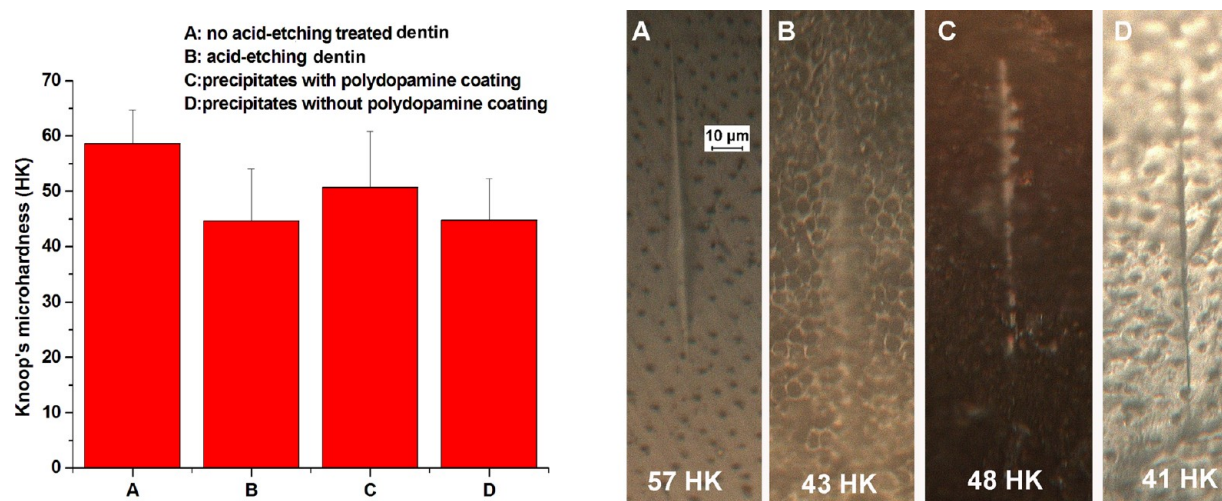

Figure 10. Knoop hardness of the dentin before and after acid-etching and acid-etched dentin after remineralization. The images were the typical indentation marks.

3.4. Mechanism of Polydopamine Coating Inducing Dental Tissue Remineralization.

Inspired by mussel-adhesion phenomena in nature, dopamine has been extensively used for biomaterial surface modification regardless of type, size, and shape of hybridized counterpart materials. Moreover, dopamine exhibits a strong adhesive property to a variety of substrates under wet conditions.[11,14,15] Dopamine self-polymerizes in situ, and catecholamines located at the interfaces are involved in the bindings. On the other hand, surface-anchored catecholamine moieties (catecholamines not participating in substrate adhesion) bind to Ca^{2+}, and enrich the interface with calcium ions, facilitating the formation of HA crystals.[16] In the present study, polydopamine binding to enamel surface may present new nucleation sites, including the still exposed HA crystal seeds. SEM results showed that the initially formed HA crystals were more packed together on enamel with polydopamine coating than that without polydopamine coating (Figure 2b and e), which suggested that the nucleation site had been changed, and enamel coating with polydopamine may be favorable for homogeneous HA nucleation. This finding obviously needs further confirmation. However, in the following remineralization process, HA crystal growth and assembly were very similar based on the SEM, XRD, and FTIR results. The hardness of the HA precipitate layer, the binding strength of the HA precipitate layer to the enamel substrate, and the interface between the precipitate layer and the enamel were almost the same. All the results confirmed that enamel coating with polydopamine presents no side effect on enamel remineralization.

On the other hand, as mentioned above that collagen matrix is ineffective in initializing HA nucleation and growth, minimal remineralization was found in demineralized dentin collagen matrix in the samples without polydopamine coating. However, for the sample of demineralized collagen fibers coated with polydopamine, remineralization was much more promoted, which implied that polydopamine binding to collagen fiber presented a new nucleation site that will be favorable for HA crystal growth. However, more differences in HA crystal growth and assembly exist between dentin remineralization (Figure 7) and enamel remineralization (Figure 3). In enamel remineralization, the HA crystals nucleated from the existing HA nucleus grew perpendicular to the enamel surface and packed densely together (Figure 3). By contrast, in dentin remineralization, the HA crystals grew more preferentially in the dentin tubules than in the peritubular dentin surface and in a separate cluster. Therefore, the mechanism of dentin remineralization is
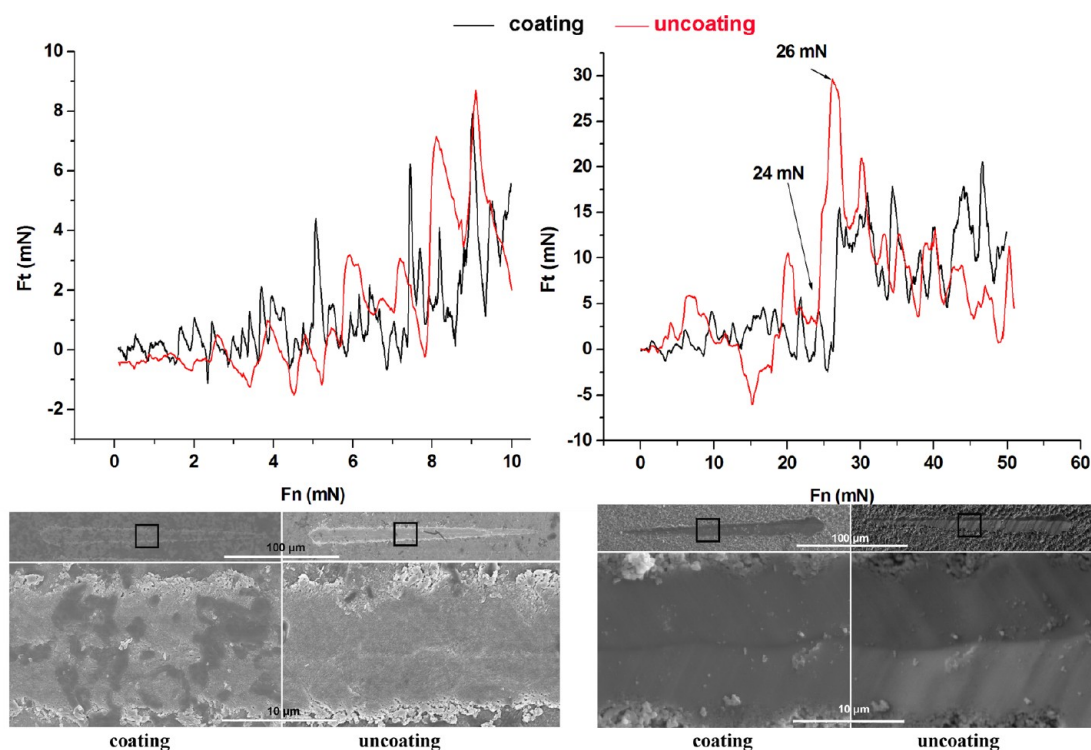
Figure 11. Correlation between frictional force (Ft) and load force (Fn) applied on the sample precipitate layer on the enamel during continuous-force nanoscratch tests.

different from that of enamel remineralization. In enamel remineralization, the mineralization substrate is mainly inorganic environment, and the crystal seeds are homogeneous HA. The precipitation crystal directly nucleated and grew on the already existing enamel HA crystals. On the other hand, the dentin remineralization substrate is collagen matrix, and its remineralization is an organic-mediated process with heterogeneous crystal seeds. In the experiment, polydopamine binding to collagen presents more new nucleation sites. The nucleation sites in the dentin tubule wall surface may have induced HA crystal nucleation and growth in spatial configuration resulting in the preferential growth of the HA crystals in the dentin tubule.

However, this method was not able to remineralize the dentin collagen fiber, especially the collagen fibers inside the collagen matrix. The method using metastable calcium and phosphate solutions for remineralization is an example of a top-down remineralization approach according to the classical crystallization theory. In this classical theory, nucleation is initiated via ion-by-ion addition to pre-existing seed crystallites, namely, epitaxial growth over existing seed crystallites. These precipitates are too large to fit into the gap zones of collagen fibrils and can only induce extrafibrillar mineral formation. Conversely, to induce collagen intrafibrillar mineralization, a bottom–up mineralization approach is needed based on the nonclassical theory of crystallization. This nonclassical theory involves the use of biomimetic analogs for generating metastable amorphous mineral precursors and mesocrystals; crystallization often proceeds via a sequential transient precursor phase transformation.[19−22] Thus, further study is necessary for inducing dentin collagen intrafibrillar mineralization.

Dentin hypersensitivity, which is a painful sensation when cool, thermal, acidic, or sweet stimulus is received by dentine exposed to mouth environment, is a common disease in clinical dentistry that is suffered by as high as 74% of the population.[2] However, to date, no desirable method has been proven to be completely effective. The ideal method for treating dentin hypersensitivity is to seal the dentin surface effectively and durably through tubule occlusion.[23] In our study, coating polydopamine on dentin was effectively able to occlude dentin tubule durably by remineralization. Thus, this method was expected to isolate the dentin surface from the stimulus as a potential therapeutic technique for dentin hypersensitivity. However, if the method was used in clinics, the biocompatibility of DOPA must be taken into consideration. Recently, polydopamine reportedly contains unpolymerized dopamine and 5,6-dihydroxyindole (DHI), the major intermediate in the process of polydopamine formation. Dopamine and DHI are potentially cytotoxic. Therefore, the polydopamine coating can be potentially toxic because of the presence of unpolymerized compounds, such as dopamine or DHI. However, this effect might not reach a toxic level because of the small amount of the unpolymerized compounds in polydopamine. Therefore, the biocompatibility of polydopamine coating should be investigated further.

4. CONCLUSION

In the present study, we used metastable calcium and phosphate solutions to remineralize enamel and dentin with and without polydopamine coating. No significant difference was found in the remineralization of enamel, whether the enamel was coated with polydopamine or not. However a significant difference was found in dentin remineralization between dentin with and without polydopamine coating. The polydopamine coating remarkably promoted demineralized dentin remineralization, and all dentin tubules were occluded by densely packed HA crystals. Thus, coating polydopamine on

dental tissue surface may be a simple universal technique to induce enamel and dentin remineralization simultaneously in the situation of metastable calcium and phosphate solutions, and it may be used as a potential therapeutic technique for dentin hypersensitivity.

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Author Contributions
Y.-Z.Z. and Y.C. contributed equally to this paper.

Notes
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