



저작자표시-비영리-변경금지 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.

다음과 같은 조건을 따라야 합니다:



저작자표시. 귀하는 원저작자를 표시하여야 합니다.



비영리. 귀하는 이 저작물을 영리 목적으로 이용할 수 없습니다.



변경금지. 귀하는 이 저작물을 개작, 변형 또는 가공할 수 없습니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#)

치의학박사 학위논문

**Mussel inspired catechol primer for
dental zirconia adhesion**

홍합 접착을 모사한 지르코니아용
카테콜 프라이머 연구

2019년 2월

서울대학교 대학원

치 의 과 학 과 치 과 생 체 재 료 과 학 전 공

박 민 수

Abstract

**Mussel inspired catechol primer for
dental zirconia adhesion**

Minsu Park, DDS

Department of Dental Biomaterials Science,

School of Dentistry, Seoul National University

(Directed by Professor Jin-Soo Ahn, DDS, Ph.D)

The aim of this study is to investigate bioinspired surface priming of catechol to zirconia. In this study, I used a bifunctional catechol-methacrylate primer, that has been reported previously to treat the surface of dental zirconia. Using the catecholic primer, in this study, we demonstrate a significant improvement in the knife shear bond strength compared to untreated surfaces.

Triethylsilyl (TES)-protected (or silylated) catechol-methacrylate was synthesized from eugenol and modified. The zirconia specimens were obtained by cutting presintered zirconia frames: yttria-stabilized tetragonal zirconia polycrystal, using a water cooled diamond saw with a 0.15 mm thick

diamond blade to 2 mm thickness and 5 mm length x 5 mm width. The specimens were then divided into five groups according to the types of used primers - Zirconia Liner (ZL), Alloy Primer (AP), Universal Primer (UP), fresh Catechol primer in methanol degassed and purged with argon, and control. SEM analysis was conducted for the primed and the non-primed zirconia surfaces. The knife-edge shear bond test was performed. The results were statistically analyzed ($\alpha = 0.05$).

The means, standard deviations of the knife-edge shear bond strengths of catechol primer on zirconia surface was higher than commercial zirconia primers containing phosphate and carboxylate methacrylates (ZL, AP, UP) and three times stronger than the control without any primer. The Tukey's test showed significant differences ($p < 0.05$) between CP and the each commercial primer. While CP showing significantly higher shear bond strength, the Tukey's post hoc analysis indicated that there was a similarity between ZL, AP, and UP.

I have then validated the superior bonding performance of the bioinspired primer to zirconia, compared to several popular commercially available dental zirconia primer. Considering the catecholic primers' higher strength and ease of application, this priming strategy is well poised for further development in dental applications requiring bonding to zirconia.

Keywords: adhesive, catechol, mussel, primer, zirconia

Student Number: 2012-30622

Contents

1. Introduction

2. Material and Methods

2.1 Synthesis of Catechol Methacrylate Primer

2.2 Zirconia Specimen

2.3 Surface Treatment

2.4 Surface Morphology

2.5 Shear Bond Strength

2.6 Statistical Analysis

3. Results and Discussion

3.1 Improved Synthesis of Catechol Methacrylate Primer

3.2 Scanning Electron Microscope (SEM) Imaging of Primed Zirconia Surface

3.3 Shear Bond Strength of Dental Adhesives on Bioinspired Catechol Primed Zirconia Surface

4. Conclusions

References

Korean Abstract

Acknowledgement

1. Introduction

In dentistry, ceramic materials have been broadly used for dental materials, e.g., for dental crowns, veneers and orthodontic brackets. Recently, zirconia has become one of the most popular ceramic dental materials with its superior mechanical properties; for example, zirconia is both chemically and dimensionally stable, thus highly tough and strong, wear resistant, shock resistant [1]. One of the most significant advantage of its superior mechanical properties of zirconia is to prevent crack propagation based on a martensitic type phase transformation [2]. However, its high chemical resistance is a double-edged sword regarding its dental applications. Traditional dental ceramic bonding techniques that use chemical etching on ceramic surface to increase bonding strengths are not compatible with zirconia due to its high chemical resistance [2]. To overcome this challenge, traditional mechanical grinding or sand blasting methods on dental ceramics have been used as an alternative, but this process causes the phase transformation and hydrothermal fatigue degradation of zirconia [3].

In adhesive techniques, priming (or adhesive priming) is a surface treatment to promote adhesion of coatings or adhesives to the substrate of interest. In dental adhesion, priming is commonly used to increase the bonding performance between dental materials or dental material and tooth surfaces. Silane-based primers (known as silane coupling agents) are the most commonly used method to prime dental surfaces, including ceramics. The role of dental methacrylate silane coupling

agents is to form a covalent bond between a -OH group on the surface of interest and the silane group of the coupling agent. Subsequently, methacrylate group on the other side of the coupling agent reacts with a methacrylate group of dental resins and adhesives. Despite many attempts to improve the bonding strength to zirconia using this methacrylate silane-based coupling agent, no significant improvement has been reported yet [3], and an alternative technique to increase the bonding strength is urgently required in dentistry.

In the past decades, the National Institute of Dental and Craniofacial Research (NIDCR) has supported interdisciplinary studies such as marine mussel adhesion as the oral environment has much in common with the intertidal environment; both oral and marine adhesions are subjected to opportunistic microbes; cyclic stress; constant fluid flow; and variations in salinity, temperature, and pH [4].

In this study, the solution was found from the nature. Figure 1 shows marine sessile organisms adhere to rocks at the seashore. Marine sessile organisms such as mussels anchor themselves using byssus at the intertidal zone where strong wave, sand and wind velocity reach up to 25 m/s [5]. The mussels use multiple proteins to adhere its byssal plaques to the wet rocky surfaces, and each specific protein has its own role. For example, mussel foot protein 1 (mfp-1) is a protective coating of the byssus; mfp-2 and mfp-4 connect between priming layer and object (byssal thread) like dental resin composites, and maintain the cohesion of the byssal plaques; mfp-3 and mfp-5 are primers. These proteins are secreted incrementally to architect the several adhesive layers as we commonly do in dentistry such as etching - priming -

adhesives – composites. I, in this study, focus on the priming adhesive proteins, i.e., mfp-3 and mfp-5, to translate the priming mechanism to the synthetic dental primers for zirconia. The mussel primer proteins contain high amount of Dopa (3,4-dihydroxy-L- phenyalanine). In synthetic approaches to mimic the wet adhesion of mussel, catechol has been used as an analog of Dopa moiety in the proteins [5].

Figure 1. Mussels and other marine sessile organisms such as mussels anchored to mineral surfaces at seashore in Santa Barbara, CA, USA.



The NIDCR's long-term investment to the bioadhesion [4,6] has recently begun to show potential for practical dental [7] and biomedical [8,9] applications. Several dental applications of catechol have been reported using catechol-containing polymers such as tannin as a dental

sealant [10] and catecholic methacrylamide for a dental adhesive [11] via catechol-ferric iron complexation. Despite the inherent aesthetic limitations of Fe-catechol complexation, (complexes are highly colored and darken over time) the previous work exposed the potential of catechol chemistry for dental materials applications. In contrast to these previous approaches which mimic the mussels' use of catecholic complexation and crosslinking chemistry for enhancement of cohesive strength within the byssus, I, in this study instead aimed to mimic the mussel's means of priming surfaces with catechol-mediated hydrogen bonding that increases the adhesive strength of mussel plaque to mineral surfaces [12].

Again, one of the useful chemical features of mussels' adhesive mechanism is the use of catechol- and phospho-rich proteins as surface primers [12-14]. This is very similar to currently dental techniques that, in dentistry, phosphorous-based primers such as 10-methacryloyloxydecyl dihydrogen phosphate (MDP) are commonly used based in part on the strength of phosphate binding to calcium ions in hydroxyapatite (the main mineral in human teeth—higher than 90 wt % in enamel and 70 wt % in dentin—and in human bone—up to 70 wt %). MDP helps to achieve bonding performance of methacrylate-based dental resins by bridging the surface minerals to a polymerizable methacrylate of dental resins.

In addition, MDP has presented its ability to improve adhesion of dental resins to zirconia surface via ionic phosphate-Zr binding [3,15], yet many researchers are still studying to discover other alternative chemistry that can fulfill the demand to further increases to the strength

of such resins bound to zirconia.

Recently, adhesion enhancement of dental adhesion to silica, steel, and tooth enamel has been reported by using the catechol-containing methacrylate primers [7,16]. In contrast to the large body of literature regarding phosphate-primers, and despite over 10,000 peer-reviewed papers published within the past decade on catechol-mediated biological adhesion [12], the use of catechol chemistry for strength enhancement and surface priming in dental settings remains largely unexplored.

Therefore, I have investigated, in this study, if one of the most pressing issues in prosthodontics — poor adhesion to zirconia — could be overcome with the catecholic bioinspired surface priming. In this study, I used a bifunctional catechol-methacrylate primer, that has been reported previously to treat the surface of dental zirconia [13]. Using the catecholic primer, in this study, I demonstrate a significant improvement in the shear bond strength compared to untreated surfaces. Moreover, the bonding performance improved by this catecholic priming technique is superior to commercial dental primers containing MDP, reliant on acidic phosphate and carboxylate functionalities. This study, therefore, highlights the potential of catechol-mediated surface priming to solve bonding issues with zirconia for dental priming applications. In addition, I correlate the superior bonding performance of the catecholic primers with its higher surface coverage; the surface coverage was investigated using scanning electron microscope (SEM). Further, I have established an improved synthetic method of the catecholic methacrylate dental primer in higher purity compared to the previously reported method [7,17,19].

2. Material and Methods

All chemicals for synthesis were purchased from Sigma-Aldrich (St. Louis, MO, USA). All dental resins and primers were purchased as shown in Table 1.

Table 1. Commercial zirconia dental primers

Primers	Composition ¹	Manufacturer
Zirconia liner (ZL)	4-META	SunMedical Co. Ltd (Shiga, Japan)
Alloy primer (AP)	10-MDP, VBATDT	Kuraray Dental, Inc. (Osaka, Japan)
Universal primer (UP)	MAC-10, MTU-6	Tokuyama Dental, Corp. (Tokyo, Japan)

¹ 4-META: 4-methacryloyloxy ethyl trimellitate anhydride; 10-MDP: 10-Methacryloyloxydecyl dihydrogen phosphate; VBATDT: 6-(4-Vinylbenzyl-n-propyl)amino-1,3,5-triazine-2,4-dithiol; MAC-10: 11-Methacryloxyundecane-1,1-dicarboxylic acid; MTU-6: 6-methacryloyloxyhexyl-2-thiouracil-5-carboxylate.

2.1 Synthesis of Catechol Methacrylate Primer

Triethylsilyl (TES)-protected (or silylated) catechol-methacrylate was synthesized from eugenol by the previously reported method [18] and generously provided to us by Osaka Organic Chemical Industry, Ltd. (Osaka, Japan). By modifying the previously reported conditions for TES-deprotection, the catecholic methacrylate could be obtained more economically, with a higher degree of purity according to the following procedure. 411 mg of TES-protected catechol methacrylate (0.855 mmol, 1 equiv.) and 229 mg of benzoic acid (1.88 mmol, 2.2 equiv., 1.1 equiv. per TES group) were dissolved in ca. 3–5 mL of tetrahydrofuran

(THF), (note: distilled/anhydrous THF was not used), and stirred at ambient temperature, whereupon a 1 M solution of tetrabutylammonium fluoride (TBAF) in THF (1.88 mL, 1.88 mmol, 2.2 equiv.) was added dropwise to the stirred mixture. The mixture was stirred at ambient temperature until thin-layer chromatography (TLC) indicates complete conversion (ca. 30–120 min). Once judged complete, the stir bar was removed, and THF was removed by rotary evaporation. The crude residue was then suspended in 150 mL of ether (Et₂O), and washed twice with DI water, once with brine, dried over sodium sulfate. Once dry, the solution was filtered and evaporated under reduced pressure, whereupon the residue was dissolved in a minimum amount of dichloromethane (DCM), loaded on top of a silica column, and purified further by flash chromatography. It should be noted that catechols adhere strongly to silica, and are subject to decomposition during chromatography, thus chromatography was performed quickly, and with a minimum amount of silica gel. Oxidative decomposition during chromatography could be mitigated by addition of a small amount (0.1% v/v) of AcOH to the eluent, although this required prolonged and undesirable amounts of time on high-vacuum to remove traces of acid. The use of silica gel impregnated with ascorbic acid was also found to reduce decomposition [20]. After eluting sequentially with 25%, then 60% EtOAc/hexanes, fractions containing desired material were then pooled in a round bottom flask, and a very small (ca. 0.1–0.4 mg) crystal of BHT as inhibitor was added, then the solution evaporated. A small quantity of DCM was used to transfer the residue to a small, tared vial, and residual volatiles were removed by repeated coevaporation of the residue with pentanes, followed by high vacuum,

to afford 147 mg (68% of theoretical) of the title compound as a clear viscous oil. The material was stored in the freezer in glass vials tightly wrapped with parafilm, and protected from light. The catechol-methacrylate primer solution was prepared as follows. First, methanol was degassed by sparging with argon for 15–30 min. The primer was removed by gently scraping some of the compound with a spatula, into a tared vial, which was then weighed, fitted with a rubber septa, and purged with argon. Sufficient degassed MeOH was then added via syringe to make a 1 mg/mL solution, the septa was then replaced with a screw cap, and the vial was vigorously vortexed for 10–20 min until no further primer could be observed adhering to the sides of the vial. Solutions were sealed tightly, protected from light, and stored in the freezer.

2.2 Zirconia Specimen

The specimens were obtained by cutting presintered zirconia frames: yttria-stabilized tetragonal zirconia polycrystal (Y-TZP, LAVA, Esthetic A3, 3M, St. Paul, MN, USA), using a water cooled diamond saw (Buehler Isomet low speed saw, model #11-1180, Buehler Ltd., Lake Bluff, IL, USA) with a 0.15 mm thick diamond blade to 2 mm thickness and 5 mm length x 5 mm width. Prior to cutting, the green bodies were presintered in a furnace at 1040 °C for 2 h. After cutting, all specimens were polished using a custom built polishing machine equipped with SiC abrasive paper #1200 in order to have the same degree of surface roughness.

2.3 Surface Treatment

I divided specimens into five groups according to the types of used primers. Each group is ZL using Zirconia Liner, AP using Alloy Primer, UP using Universal Primer, CP using fresh catechol primer (0.1 mg/mL) in methanol (anhydrous, 99.8%) degassed and purged with argon [17] to avoid catecholic auto-oxidation [17], and control (non-treated specimen, negative control). The primers were applied according to the manufacturer's instructions.

2.4 Surface Morphology

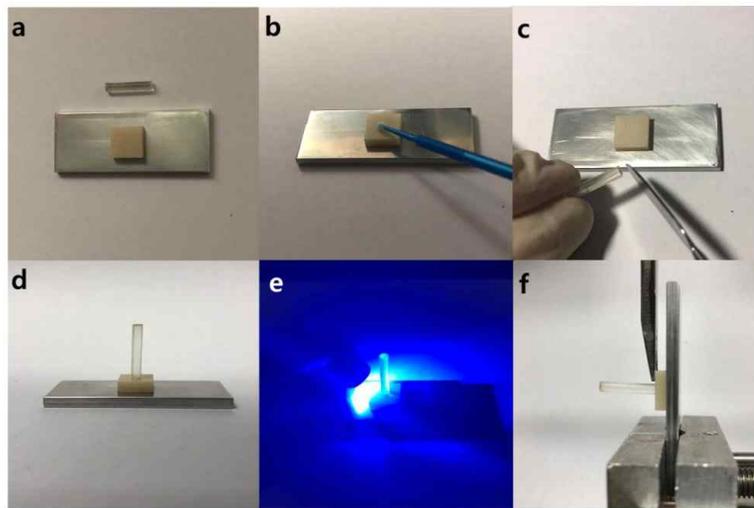
SEM analysis was conducted for the primed (surface-coated with primers) and the non-primed zirconia surfaces. To prepare the primed samples, the commercial primers were applied on the surfaces as directed in the manuals provided by the manufacturers. Catechol primer solution was applied according to the previous report [17]. The surface images were collected using field emission scanning electron microscope (FESEM, Hitachi S-4700, Hitachi Co., Tokyo, Japan) at two different magnifications (x250, x1000).

2.5 Shear Bond Strength

Shear bond test was conducted based on previous reports [7,17,21] using a modified ISO/TS 11405: 2015 as shown in Figure 2. Briefly, a cured dental resin rod 2.5 mm in diameter shown in Figure 2 was prepared using a common dental monomer mixture (49.5 wt % of

Bis-GMA, 49.5 wt % of TEGDMA, and 1.0 wt % of DMAEMA and CQ mixture at 1:2 molar ratio). The bottom of the rod was polished and leveled flat with #800 SiC abrasive paper to obtain the same surface roughness. Dental resin cement (Bisco, Schaumburg, IL, USA) was then applied onto the bottom surface of the rod (Figure 2c) as to simulate the bottom of the resin. The rod was then placed on the primer-treated zirconia surface at orthogonal to the surface and lightly pushed (Figure 2d). The excess of resin cements at the edge of rods was removed using a dental wax carver to avoid gluing on the side wall of rods prior to the light curing. Subsequently, blue light (Demi™ Ultra Dental Curing Lights, Kavo Kerr, Orange, CA, USA) was applied all around surface for the complete cure for 20–40s (Figure 2e). All specimens were stored in water at room temperature for 24 h prior to bonding strength testing. Shear bond test was performed at crosshead down speed of 1 mm/min (Figure 2f) by a universal testing machine (UTM 4465, Instron, Norwood, MA, USA). Note that a contribution of the bending moment of the rod was diminished by applying the stress at the bottom surface of the rod (at the interface between substrate and rod). Each test was repeated 10 times with 10 specimens ($n = 10$); average and standard deviation were calculated.

Figure 2. Images taken during sample preparation: (a) a zirconia sample adhered to a stainless-steel plate; (b) apply primer solutions on the zirconia surface; (c) dental resin cement applied to the bottom of resin rod; (d) the resin rod placed on the surface; (e) light curing; (f) shear bond test.



2.6 Statistical Analysis

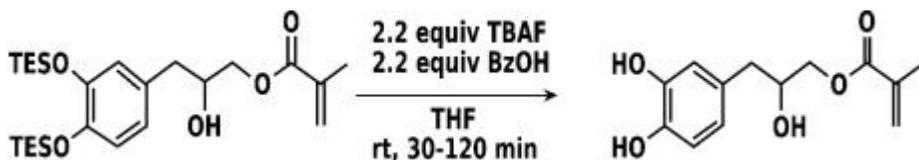
Shear bond test data were analyzed using a one-way ANOVA followed by a Tukey's post hoc test at a 5% level of significance (SPSS 25.0; SPSS Inc., Chicago, IL, USA).

3. Results and Discussions

3.1 Improved Synthesis of catechol Methacrylate Primer

In the previous study, the preparation of the catecholic methacrylate primers remains my concerns and encountered some difficulties in the previously reported TES-deprotection method [7]. The prior method involved the use of tetrabutylammonium fluoride (TBAF) as limiting reagent, and an excess of the more valuable TES-protected intermediate, the reaction apparently being driven to completion by reaction with adventitious water. Since the prior procedure required that TBAF be used without a buffer, phenolic groups are liable to stay ionized and in the aqueous phase without an acidic workup. Additionally, since the previous conditions are basic due to the use of fluoride anion; catechol moieties are susceptible to auto-oxidation, resulting in lower yields, yellow sample coloration, and baseline impurities. These basic conditions also apparently are the origin of the observed migration of some of the methacrylates to the internal secondary alcohol, as visible in the proton NMR. In this study, I have increased the yield, purity, and reproducibility of this silyl-deprotection by buffering the TBAF in the reaction mixture with an equimolar amount of benzoic acid (Scheme 1). The Scheme 1 shows the new chemical synthetic route to synthesize the catecholic methacrylate primer.

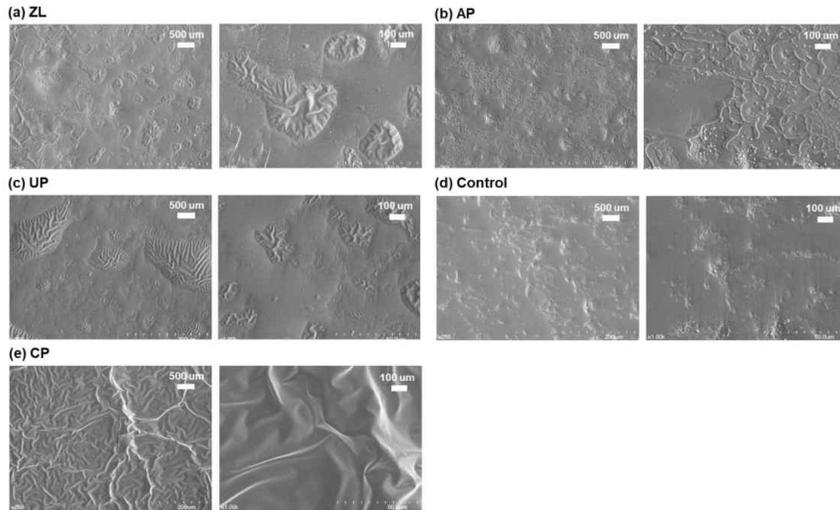
Scheme 1. Synthetic scheme of catechol methacrylate from silyated eugenol.



3.2 Scanning Electron Microscope (SEM) Imaging of Primed Zirconia Surface

Surface morphology of zirconia surfaces with and without primer treatments was studied with a SEM (Figure 3). In the SEM study, CP containing catechol methacrylate shows a complete coverage of zirconia surface, whereas the commercial zirconia primers (ZL, AP, and UP) containing phospho- and/or carboxyl-methacrylates show partial coating on zirconia surfaces. I predicted that higher surface coverage would be positively correlated with the adhesive performance of dental resins to zirconia surface, by allowing for greater microscopic contact areas (reducing microscopic gaps) between zirconia and resin, which was subsequently supported by the results of the shear bond tests (vide infra).

Figure 3. SEM images of zirconia surfaces primed with: (a) ZL: zirconia liner; (b) AP: alloy primer; (c) UP: universal primer; (d) control: no primer; (e) CP: catechol primer.



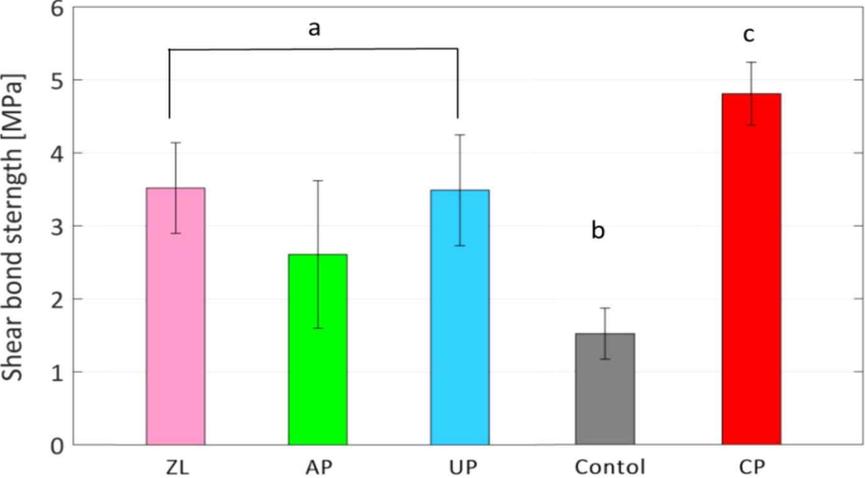
3.3 Shear Bond Strength of Dental Adhesives on Bioinspired Catechol Primed Zirconia Surface

Shear bond test was conducted to measure bonding performance of dental adhesives on zirconia surface. Failure mode of each bonding test after the test was monitored by an optical microscope(SZ61, Olympus, Tokyo, Japan), and all the failure occurred on zirconia surface as anticipated. The means, standard deviations of the shear bond strengths are shown in Figure 4. with the complete surface coverage of CP on

zirconia surface shown in SEM analysis in Figure 3, the shear bond of CP ($4.81 \text{ MPa} \pm 0.43$, $n = 10$; the mean of maximum shear strength, \pm as standard deviation, and the n is number of experiments) was higher than commercial zirconia primers containing phosphate and carboxylate methacrylates, i.e., ZL ($3.52 \text{ MPa} \pm 1.01$, $n = 10$), AP ($2.61 \text{ MPa} \pm 0.76$, $n = 10$) and UP ($3.49 \text{ MPa} \pm 1.03$, $n = 10$), and three times stronger than the control without any primer ($1.52 \text{ MPa} \pm 0.35$, $n = 10$).

The statistical certainty of the comparison was confirmed by one-way ANOVA with post hoc test. The Tukey's test showed significant differences ($p < 0.05$) between CP (group c in Figure 4) and the each commercial primer (in group a in Figure 4); p value of CP to ZL was 0.014, that of CP to AP was 0.000 and that of CP to UP was 0.012. While CP showing significantly higher shear bond strength than group a and group b (negative control), the Tukey's post hoc analysis indicated that there was a similarity between ZL, AP, and UP (group a) in Figure 4.

Figure 4. Shear bond strength of ZL, AP, UP, control (no primer), and CP.



4. Conclusions

Improving the bonding strength of zirconia surface has been a great challenge in dentistry. In this study, I have found the inspiration from nature, i.e., marine sessile organisms. In this study, I have replicated one of the marine mussel's adhesion mechanisms, specifically its priming mechanism on mineral surfaces using catechol moieties in its primer proteins such as mfp-3 and mfp-5. By using a synthetic small molecule containing methacrylate and catechol groups, I have successfully coat and prime zirconia surfaces. My strategy was to tether a polymerizable methacrylate to a catechol moiety to produce a coupling agent. I have then validated the superior bonding performance of the bioinspired primer to zirconia, compared to several popular commercially available dental zirconia primers. SEM imaging shows that in contrast to those utilizing acidic monomers, the catecholic primer provides a much greater degree of surface coverage, which is correlated with the observed enhancement in dental bonding performance.

Considering the catecholic primers' higher strength and ease of application, this priming strategy is well poised for further development in dental applications requiring bonding to zirconia. If I could have accomplished a rapid underwater curing and more durable underwater adhesion in addition to this strong zirconia bonding that I present here, it would be more interesting. Therefore, I will continue to work on this topic of wet-bonding and underwater curing for dental and biomedical applications. This biomimetic priming strategy for stronger dental zirconia bonding can contribute to the field of dental adhesion and can encourage other researchers to further study to understand the zirconia

priming mechanisms and develop good biomimetic adhesion technologies.

References

1. Piconi, C.; Maccauro, G. Zirconia as a ceramic biomaterial. *Biomaterials* 1999, 20, 1–25.
2. Paes, P.N.G.; Bastian, F.L.; Jardim, P.M. The influence of Y-TZP surface treatment on topography and ceramic/resin cement interfacial fracture toughness. *Dent. Mater.* 2017, 33, 976–989.
3. Chuang, S.-F.; Kang, L.-L.; Liu, Y.-C.; Lin, J.-C.; Wang, C.-C.; Chen, H.-M.; Tai, C.-K. Effect of silane- and MDP-based primers application orders on zirconia-resin adhesion—A ToF-SIMS study. *Dent. Mater.* 2017, 33, 923-933.
4. Holten-Andersen, N.; Waite, J.H. Mussel-designed protective coatings for compliant substrates. *J. Dent. Res.* 2008, 87, 701–709.
5. *J. Am. Chem. Soc.*, 2017, 139 (30), pp 10166–10171 DOI: 10.1021/jacs.6b13149
6. Rodriguez, N.R.M.; Das, S.; Kaufman, Y.; Wei, W.; Israelachvili, J.N.; Waite, J.H. Mussel adhesive protein provides cohesive matrix for collagen type-1. *Biomaterials* 2015, 51, 51–57.
7. Seo, S.; Lee, D.W.; Ahn, J.S.; Cunha, K.; Filippidi, E.; Ju, S.W.; Shin, E.; Kim, B.S.; Levine, Z.A.; Lins, R.D.; et al. Significant performance enhancement of polymer resins by bioinspired dynamic bonding. *Adv. Mater.* 2017, 29, 703026.
8. Kastrup, C.J.; Nahrendorf, M.; Figueiredo, J.L.; Lee, H.; Kambhampati, S.; Lee, T.; Cho, S.W.; Gorbato, R.; Iwamoto, Y.; Dang, T.T.; et al. Painting blood vessels and atherosclerotic plaques with an adhesive drug depot. *Proc. Nat. Acad. Sci. USA* 2012, 109, 21444–21449.

9. Kiveliö, A.; Dekoninck, P.; Perrini, M.; Brubaker, C.E.; Messersmith, P.B.; Mazza, E.; Deprest, J.; Zimmermann, R.; Ehrbar, M.; Ochsenein-Koelble, N. Mussel mimetic tissue adhesive for fetal membrane repair: Initial in vivo investigation in rabbits. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2013, 171, 240–245.
10. Oh, D.X.; Prajatelista, E.; Ju, S.-W.; Jeong Kim, H.; Baek, S.-J.; Joon Cha, H.; Ho Jun, S.; Ahn, J.-S.; Soo Hwang, D.S. A rapid, efficient, and facile solution for dental hypersensitivity: The tannin–iron complex. *Sci. Rep.* 2015, 5, 10884.
11. Lee, S.-B.; González-Cabezas, C.; Kim, K.-M.; Kim, K.-N.; Kuroda, K. Catechol-functionalized synthetic polymer as a dental adhesive to contaminated dentin surface for a composite restoration. *Biomacromolecules* 2015, 16, 2265–2275.
12. Ahn, B.K. Perspectives on mussel-inspired wet adhesion. *J. Am. Chem. Soc.* 2017, 139, 10166–10171.
13. *J. Am. Chem. Soc.*, 2015, 137 (29), pp 9214–9217 DOI: 10.1021/jacs.5b03827
14. Danner, E.W.; Kan, Y.J.; Hammer, M.U.; Israelachvili, J.N.; Waite, J.H. Adhesion of mussel foot protein Mefp-5 to mica: An underwater superglue. *Biochemistry* 2012, 51, 6511–6518.
15. Ahn, B.K.; Das, S.; Linstadt, R.; Kaufman, Y.; Martinez-Rodriguez, N.R.; Mirshafian, R.; Kesselman, E.; Talmon, Y.; Lipshutz, B.H.; Israelachvili, J.N.; et al. High-performance mussel-inspired adhesives of reduced complexity. *Nat. Commun.* 2015, 6, 8633.

16. Rickman, R.D.; Verkhoturov, S.V.; Balderas, S.; Bestaoui, N.; Clearfield, A.; Schweikert, E.A. Characterization of surface structure by cluster coincidental ion mass spectrometry. *Appl. Surf. Sci.* 2004, 231, 106–112.
17. Shin, E.; Ju, S.W.; An, L.; Ahn, E.; Ahn, J.-S.; Kim, B.-S.; Ahn, B.K. Bioinspired catecholic primers for rigid and ductile dental resin composites. *ACS Appl. Mater. Interfaces* 2018, 10, 1520–1527.
18. Ahn, B.K.; Lee, D.W.; Israelachvili, J.N.; Waite, J.H. Surface-initiated self-healing of polymers in aqueous media. *Nat. Mater.* 2014, 13, 867–872.
19. Seo, S.; Das, S.; Zalicki, P.J.; Mirshafian, R.; Eisenbach, C.D.; Israelachvili, J.N.; Waite, J.H.; Ahn, B.K. Microphase behavior and enhanced wet-cohesion of synthetic copolyampholytes inspired by a mussel foot protein. *J. Am. Chem. Soc.* 2015, 137, 9214–9217.
20. Gelbke, H.P.; Knuppen, R. A new method for preventing oxidative decomposition of catechol estrogens during chromatography. *J. Chromatogr. A* 1972, 72, 465–471.
21. Lee, J.-H.; Lee, M.; Kim, K.-N.; Hwang, C.-J. Resin bonding of metal brackets to glazed zirconia with a porcelain primer. *Korean J. Orthod.* 2015, 45, 299–307.

국문요약

홍합 접착을 모사한 지르코니아용 카테콜 프라이머 연구

서울대학교 대학원 치의과학과 치과생체재료과학 전공

(지도교수 안 진 수)

박 민 수

이 연구는 생물모사된 카테콜 프라이머의 지르코니아에 대한 전처리효과를 알아보기 위한 것이다. 실험을 위해 치과용 지르코니아 표면처리에 사용된 것으로 보고된 bifunctional catechol-methacrylate primer를 이용하였다. 이번 연구를 통하여, 카테콜 프라이머를 적용한 경우가 그렇지 않은 경우와 비교했을 때 전단결합강도가 상당히 우수함을 확인할 수 있었다.

Triethylsilyl (TES)-protected (or silylated) catechol-methacrylate 은 유지놀로부터 합성하였고 일련의 조절 과정을 거쳤다. 지르코니아 시편은 소결되지 않은 지르코니아 (yttria-stabilized tetragonal zirconia polycrystal) 를 주수 하에 0.15 mm 두께의 다이아몬드 날을 가진 톱으로, 2 mm 두께와 5 mm x 5 mm의 길이와 너비를 갖도록 절삭하여 준비하였다. 그 다음, 시편을 프라이머에 따라 5개 군으로 나누었다 (Zirconia Liner (ZL), Alloy Primer (AP), Universal Primer (UP), catechol primer (CP), 대조군). 전처리 전 후의 지르코니아 표면을 비교하기 위해 SEM 분석을 진행하였다.전단

결합강도실험을 시행하였고 이 결과를 통계적으로 분석하였다.($\alpha = 0.05$)

지르코니아 표면에 카테콜 전처리를 한 쪽의 전단결합강도의 평균값과 표준편차가 phosphate와 carboxylate methacrylates를 함유하고 있는 다른 상용 지르코니아 프라이머 보다 높았고, 아무런 전처리를 하지 않은 대조군 보다는 3배 높은 수치를 보여주었다. Tukey's test 결과 카테콜 프라이머와 여타 상용 프라이머 사이에 상당한 차이가 있었다 ($p < 0.05$). 카테콜 프라이머는 다른 프라이머 및 대조군 보다 월등히 높은 전단결합강도 수치를 보였지만, 사후 검정 결과 ZL, AP, UP 사이에는 큰 차이가 없었다.

이번 연구를 통해 생물모사된 카테콜 프라이머는 지르코니아 접착을 위해 현재 널리 사용중인 타 프라이머 대비 우수한 본딩력을 보여주었다. 카테콜 프라이머는 지르코니아에 대한 높은 본딩력을 갖고 있으면서도 그 적용이 어렵지 않기 때문에 지르코니아를 치과영역에서 사용하기 위해 필요한 전처리법을 개발하는 데 있어 좋은 방법이 될 수 있다.

주요어: adhesive, catechol, mussel, primer, zirconia

학번: 2012-30622