

Effect of Silver Nanoparticles, Zinc Oxide Nanoparticles and Titanium Dioxide Nanoparticles on Microshear Bond Strength to Enamel and Dentin

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ABSTRACT

Aim: This study was aimed to evaluate whether antibacterial pretreatment of enamel and dentin with silver nanoparticles (SNPs), zinc oxide nanoparticles (ZNPs) and titanium dioxide nanoparticles (TNPs) has any effect on the microshear bond strength of an etch-and-rinse adhesive system.

Materials and methods: Eighty human third molars were randomly assigned to eight subgroups ($n = 10$). Enamel groups included no pretreatment (E), pretreatments with SNPs (ESNP), ZNPs (EZNP) and TNPs (ETNP) before acid etching and adhesive application. Dentinal groups included no pretreatment (D), pretreatments with SNPs (DSNP), ZNPs (DZNP) and TNPs (DTNP). The specimens were bonded by Adper Single Bond and polyvinyl chloride microtubes and were restored with Z250 composite. The bonded surfaces underwent microshear bond strength (μ SBS) test. Data in megapascal (MPa) were analyzed with the Kruskal–Wallis test and the Mann–Whitney test ($p = 0.05$).

Results: There was not a significant difference among the groups in enamel ($p > 0.05$). There was no significant difference between the application of three nanoparticles and the control group in dentin. However, DSNPs had a higher μ SBS (25.60 ± 14.61) than that of the DZNPs and DTNPs groups ($p = 0.03$ and $p = 0.001$, respectively). Also, the mean μ SBS value was lower in dentin groups compared to the respective enamel groups ($p < 0.05$) except for groups DSNPs and ESNPs in which no significant difference was found ($p > 0.05$).

Conclusion: Pretreatment with SNPs, TNPs, and ZNPs can be suggested to achieve potent antibacterial activities without compromising the bond strength. The best result was obtained for pretreatment with SNPs compared to pretreatment with TNPs or ZNPs in dentin and enamel, albeit the differences were not significant in the enamel groups.

Clinical significance: Effective antibacterial treatment prior to adhesive bonding application is desirable to provide successful restoration if it would not adversely affect the bond strength of the adhesive system. Nanoparticles can be applied to meet this goal.

Keywords: Adhesive bonding, Laboratory research, Microshear bond strength, Nanoparticles.

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INTRODUCTION

Despite their advantages and their extensive use in the dental clinical practice, resin composites still present some limitations that impair their clinical performance. The principal shortcoming of them include the development of recurrent caries at the composite resin-tooth interface which is often cited as the main reason for replacement of composite restorations.^{1,2} Nowadays, minimally invasive techniques have been advocated for removing the infected-dentin, leaving behind the caries-affected tissue in the cavity.³ Therefore, residual bacteria may still be present in the prepared tooth cavity when the tissue affected by caries is not fully removed and microleakage may allow bacteria to invade the tooth-restoration interfaces during service.⁴ This may lead to the colony growth of bacterial species, especially

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S. mutans, under the restoration, secondary caries and consequently reduced longevity of the restorations.⁵ Therefore, some attempts have been made to hinder bacterial invasion and growth such as incorporating antibacterial agents into adhesives, primers, and composite resins.^{1,6,7} Although different bacteriostatic and bactericide chemicals such as chlorhexidine, Ag-salts and particles, and oxides have been previously incorporated into composite resins to confer antibacterial activity to them, they could potentially jeopardize the composites' physicochemical properties.^{7,8} Moreover, a recent study found that the incorporation of various nanoparticles into adhesive materials may have negative effects on the shear bond strength.⁹ Besides adding active antimicrobial ingredients to the dental materials, another strategy for bacterial reduction is coating surfaces with antibacterial agents to create anti-adhesive surfaces.^{10,11}

Recently, nanomaterials referring to the materials with a size of less than 100 nm have captured more attention from researchers in dentistry because of their unique properties and structures such as small size, large surface area, a large proportion of surface atoms and high surface energy.¹² In this regard, different metal NPs have been used in various dental branches because of their antibacterial properties. Moreover, bacteria are less likely to develop resistance against metal nanoparticles than a majority of commercially available antibiotics.¹³ Silver nanoparticles (SNPs) has been investigated in dentistry mainly because of their long-term antibacterial property via sustained silver ion release. SNPs have exhibited broad-spectrum antibacterial and antiviral properties in low concentrations related to the multiple antibacterial mechanisms of silver such as the loss of the integrity of bacterial cell membrane and increased cell wall permeability caused by adherence and penetration into the bacterial cell wall, loss of DNA replication ability and inactivation of the vital enzymes of bacteria leading to cell death.^{14,15} Also, it has been shown that SNPs have 25-folds higher antibacterial efficacy than chlorhexidine.¹⁶ Moreover, biocompatibility of SNPs especially in a lower concentration has been confirmed previously.¹⁷ A recently published study indicated that an additional pretreatment with SNPs had positive effects on the bond strength of etch-and-rinse and self-etch adhesives with the best results reported for Adper Single Bond and before acid etching.¹¹

Similar to SNPs, ZNPs have exhibited antibacterial effects against several types of gram-negative and gram-positive bacteria, including *S. mutans* and *Lactobacillus* in dental plaque.^{18,19} In fact, ZNPs have demonstrated selective toxicity against bacteria with minimal effects on human cells.²⁰ ZNPs provide the antibacterial effect by modification of cell membrane activity and oxidative

stress.²¹ Another nanoparticle, which has been recently used in dentistry, is titanium dioxide (TiO₂) TNP. Beside their bactericidal effects, TNPs have pleasing color and high biocompatibility.^{6,22} Also, better antibacterial properties compared to chlorhexidine have been shown for TNPs.¹⁶

Recently, application of metal-based nanoparticles to improve bond strength properties of composite resins has attracted more attention.^{11,13} To the authors' knowledge there are no published studies that address the effect of SNPs, ZNPs and TNPs pretreatments on the bond strength of the composite resin to enamel and dentin. The inherent bactericidal property of NPs has prompted us to investigate the role of SNPs, ZNPs and TNPs pretreatments on the microshear bond strength of the composite resin to enamel and dentin in the present study.

MATERIALS AND METHODS

After approval of the study design by the ethics committee for research of Shiraz University of Medical Sciences, eighty caries-free extracted human third molars were collected from 20 to 35-year-old patients, cleaned with a periodontal curette and stored in 0.5% chloramine solution at 4°C for no longer than 1 month until use. The teeth were previously examined under a stereoscopic microscope (Carl Zeiss, Oberkochen, Germany) for the absence of the structural deformities, abrasion, fracture, crack and previous restorations. The roots were removed from the crown in all the specimens. Forty teeth were prepared for testing the μ SBS to enamel (E). After preparing 0.5 mm deep, flat enamel surfaces at the midbuccal aspects of the teeth using diamond fissure burs (Diamond fissure 330; SS White) in a high-speed handpiece under sufficient water cooling, the teeth were embedded in acrylic resin with the buccal surfaces upward and parallel to the base of the resin block. The buccal surfaces were slightly wet-ground with 320-grit silicon carbide papers to obtain standardized flat enamel surfaces. A stereoscopic microscope (Carl Zeiss, Oberkochen, Germany) was used to check for the absence of dentin on the enamel surfaces. Another forty teeth were prepared for performing the μ SBS tests on dentin (D). Dentin substrate specimens were prepared by sectioning the crowns using a water-cooled low-speed cutting machine (Mecatome T201 A, Presi, Grenoble, France) perpendicular to the long axis of the tooth to expose the flat, midcoronal dentin surfaces by removing the occlusal enamel and the superficial dentin. The sectioned teeth were mounted in acrylic resin (Acropars; Marlik Co., Tehran, Iran) with the dentin surfaces oriented perpendicular to the bottom of the mold. To create a uniform smear

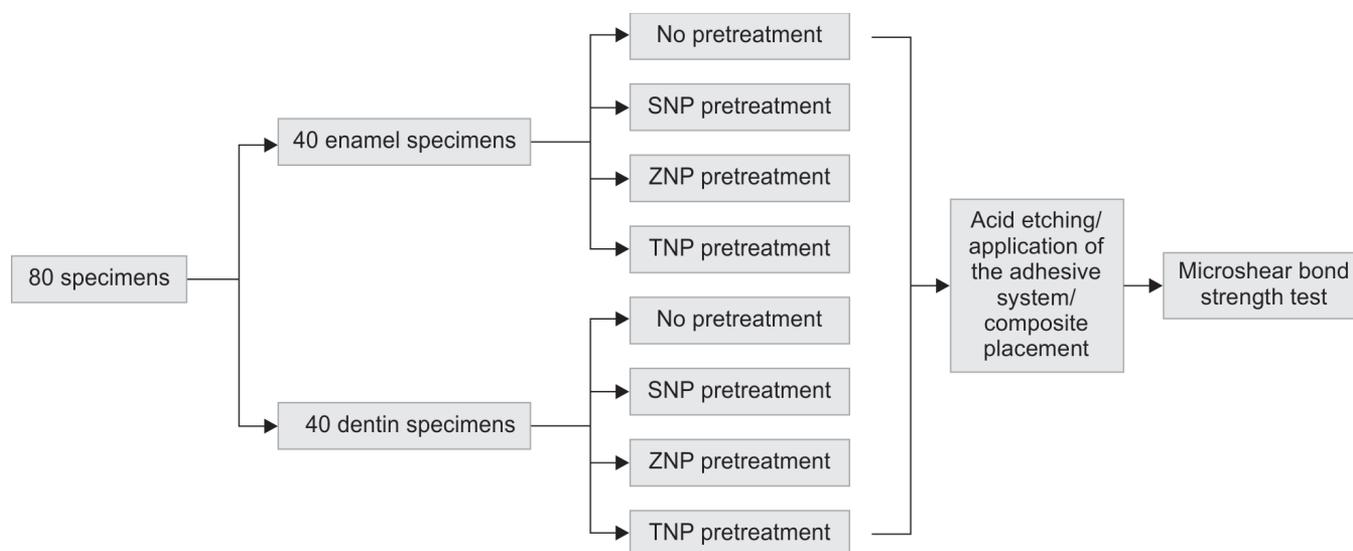


Fig. 1: Diagram of experimental design

layer, the dentin surfaces were slightly wet-ground with 320-grit silicon carbide papers for 1 minute, rinsed and dried with an air-water syringe.

Enamel and dentin samples were randomly divided into four subgroups based on three antibacterial dentin pretreatments with SNPs, ZNPs and TNPs (purchased from US-Nano materials Inc., USA) with an equal number of samples per group ($n = 10$). The sizes of the NPs were 20 nm for SNPs and TNPs and 10 to 30 nm for ZNPs. In the control groups (no treatment; D and E), Adper Single Bond (SB, 3M ESPE) adhesive system was used according to the manufacturer's instructions. In groups, ESNPs and DSNPs, surface pretreatment with SNPs was done for one minute before acid etching, and then the dentin or enamel surface was rinsed thoroughly for one minute. Surface pretreatment with ZNPs solution was done in groups EZNPs and DZNPs. Groups ETNPs and DTNPs received surface pretreatment with TNPs solution before acid etching.

Prior to light curing of the adhesives, a piece of translucent polyvinyl chloride microtubes 0.7 mm in internal diameter and approximately 0.5 mm height was placed on the bonding surface defined by an adhesive tape with a punched hole over the center of the flattened enamel or dentin surface and subsequently filled with Z250 composite (3M ESPE, St Paul, MN, USA). Light curing was performed using a light curing unit (VIP Junior, Bisco, Schaumburg, IL, USA) at 600 mW/cm^2 . The diagram of the experimental design is shown in Figure 1. The bonded specimens were stored in distilled water at 37°C for 24 hours and then were placed in a jig attached to a universal testing machine (Instron, Z020. Zwick Roell, Germany). A shear force was applied to each specimen with a direction parallel to the bonded interface at a crosshead speed of 0.5 mm/minute , as is shown in Figure 2, until failure occurred. The μSBS values in MPa were

calculated by dividing the recorded load at failure by the bonded surface area. Failure mode analysis was performed by examining the debonded specimens under a stereomicroscope (Carl Zeiss Inc., Oberkochen, Germany) at $\times 40$ and categorized as follows: (A) adhesive failure within the adhesive interfacial zone; (B) cohesive failure in the composite/enamel or dentin; and (C), mixed adhesive failure and cohesive failure. The data were subjected to the Kruskal-Wallis test to compare the groups followed by the Mann-Whitney test for paired comparisons using Statistical Package for the Social Sciences (SPSS) version 17 software (SPSS Inc, Chicago, USA) ($p < 0.05$).

RESULTS

Mean μSBS and standard deviation (MPa) for the eight groups are presented in Table 1. According to the results

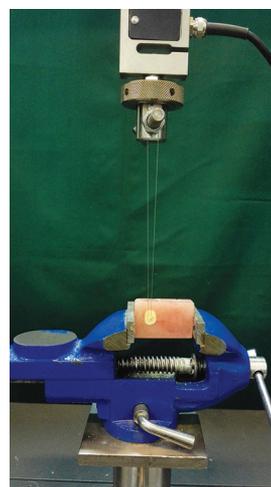


Fig. 2: Stainless steel ligature wire wrapped around the base of resin comitemicro-cylinderbonded to the specimen that is attached to the jig of the universal testing machine

Table 1: μ SBS for each group (MPa \pm SD)

	Groups			
	Control (no pretreatment)	SNPs pretreatment	TNPs pretreatment	ZNPs pretreatment
Enamel	46.74 \pm 12.18	40.56 \pm 14.45	34.40 \pm 10.95	39.91 \pm 15.02
Dentin	13.70 \pm 5.89	25.60 \pm 14.61	8.80 \pm 3.07	14.76 \pm 10.44

Table 2: Fracture modes to enamel and dentin

	Groups											
	Control (no pretreatment)			SNPs pretreatment			TNPs pretreatment			ZNPs pretreatment		
	A	C	M	A	C	M	A	C	M	A	C	M
Enamel	1	2	7	2	1	7	1	0	9	2	1	7
Dentin	1	1	8	1	1	8	2	1	7	1	0	9

Modes of failure: A–Adhesive failure; C–Cohesive failure; M–Mixed

of Kruskal–Wallis test, there was not a significant difference among the groups in enamel ($p > 0.05$) meaning that the application of three nanoparticles revealed no adverse effect on μ SBS to enamel. However, the Kruskal–Wallis test showed significant differences among the four groups in dentin ($p = 0.012$). Despite higher μ SBS obtained in the DSNPs group compared to those of the control group, this difference was not statistically significant ($p > 0.05$). There was no significant difference between the application of three nanoparticles and the control group in dentin. However, the Man–Whitney test revealed that DSNPs had a higher μ SBS (25.60 \pm 14.61) than that in the DZSNPs and DTNPs groups ($p = 0.03$ and $p = 0.001$, respectively). Also, the pairwise comparison showed that μ SBS was lower in dentin groups compared to the respective enamel groups ($p < 0.05$) except for groups DSNPs and ESNPs in which no significant difference was found ($p > 0.05$). Moreover, fracture analysis revealed that mixed failure was the most common type of observed failure (Table 2).

DISCUSSION

Nanotechnology and nanomaterials represent an area of investigation that has recently attracted much attention in dentistry and resulted in opening up new ways to benefit patients.¹² Metal-based nanoparticles such as SNPs, TNPs, and ZNPs have been used in various medical and dental branches because of their antibacterial properties.^{6,14,18} This study was conducted to evaluate the effect of enamel and dentin pretreatment with SNPs, TNPs, and ZNPs on the μ SBS of an etch-and-rinse adhesive. The results of the current study showed that the application of SNPs, ZNPs, and TNPs revealed no adverse effect on μ SBS to enamel and dentin. Although no significant difference was observed among the application of different nanoparticles in enamel, SNPs showed better results compared to TNPs and ZNPs in dentin. Also, no detrimental visual effect on the color of composite resins was observed for

nanoparticles used in this study although the samples were not examined under a stereomicroscope. The mean μ SBS for the DSNPs was more than that of the control group, albeit the difference was not significant. It seems that the SNP application had a positive effect on wetting the dentin surface and subsequent infiltration of the bonding agent. Moreover, the least values of mean μ SBS were observed after pretreatment with TNPs in enamel and dentin although the differences were not significant. The μ SBS was lower in dentin groups compared to the respective enamel groups ($p < 0.05$) except for the groups DSNPs and ESNPs which did not reveal a significant difference among them.

There are two broad mechanisms for using the antibacterial properties of nanoparticles in the oral cavity to reduce the biofilm formation. The first one is combining dental materials with NPs and the second one is coating surfaces with NPs to prevent microbial adhesion. The second mechanism was used in the current study.^{11, 23, 24}

The microshear bond test has been used in the current study to evaluate the bond strength of the dental adhesive to the tooth structure. The microshear test is a reliable and facile method which has overcome the drawbacks of the macroshear test, including inhomogeneous distribution of stress in the area over which the load is applied, the occurrence of the failure in the dentinal substrate at much lower stresses than the substrate strength and the mixed loading mode.²⁵

Residual bacteria resulting from incomplete removal of the caries lesion from cavity walls may lead to pulp damage and recurrent caries.²⁶ Less removal of tooth structure and minimal intervention dentistry have become more popular recently leading to the increased possibility of leaving more carious tissues in tooth cavity containing active bacteria.^{3,4} Moreover, studies showing microgaps at tooth-restoration interfaces confirm that a complete sealing of the tooth-restoration interface is difficult to achieve in clinical practice, and microgaps may

be created at the margins as the results of polymerization shrinkage combined with wear and chewing stresses.^{27,28} Therefore, an antibacterial surface pretreatment directly contacting enamel and dentin surface could be beneficial to help disinfect the prepared tooth cavity, eradicate the residual bacteria and combat the new invading bacteria along the tooth-restoration margins. Considering these facts, different cavity disinfectants such as peroxide or chlorhexidine have been used previously by dental practitioners in the treatment of caries because of the difficulty in determining complete removal of the caries lesion from the prepared cavity.²⁶ An important point which should be considered when choosing a cavity disinfectant is that an ideal cavity disinfectant should provide effective antibacterial action without having an adverse effect on the bond strength of adhesive systems to enamel and dentin.²⁵ However, it was indicated that pretreatment with traditional cavity disinfectants may negatively affect the bond strength of adhesive systems.²⁹ Another concern about the use of cavity traditional disinfectants is that they may not exhibit long-term antibacterial effects or may not completely remove the viable microorganisms in the prepared cavity walls.³⁰

Silver is an important broad-spectrum antibacterial, and an antiviral agent which exhibits long-term antibacterial property via sustained silver ion release, a low bacterial resistance compared to antibiotics, good biocompatibility with human cells and a low toxicity.^{13-15,17} The exact bactericidal mechanism of silver is not fully understood. Some possible explanations are as follows: (a) silver causes structural damage in the bacteria by oxygen changing into active oxygen (ROS and hydroxyl radicals), (b) the released biologically active silver ions which can interact with biological molecules inhibit DNA's ability to replicate, (c) The direct contact of the particles with the cell wall results in releasing a very high concentration of silver ions in a small area and killing the cell. The last mechanism is responsible mainly for antibacterial activity of entrapped SNPs in resin materials.^{14,15,31} These properties have encouraged SNP application in dentistry such as incorporation of SNPs into dental resins.^{5,24} An important problem regarding incorporation of SNPs into dental resins is the possible adverse effect of the SNPs on the resin color, mechanical properties, and the polymerization process.^{31,32} Moreover, a much higher antibacterial activity was shown by silver nanoparticles (25 nm) compared with zinc oxide (125 nm) and gold (80 nm) nanoparticles in a previous study which might be attributed to the size of applied nanoparticles.³³ Although the antimicrobial effect of silver against *S. mutans* has been previously demonstrated, this effect was not present for the SNPs incorporated into the resin

cement. An explanation for this finding is that SNPs have a high propensity for aggregation, which decrease the surface energy and consequently antibacterial effect. Moreover, incorporation of SNPs into dental resins result in their entrapment in the specimens resin and decreased elution of the particles from the specimens after polymerization, making the direct contact of SNPs with the bacteria minimal and consequently no or very small remained antibacterial effect.³¹ Considering this discussion, to prevent microbial adhesion, we applied nanoparticles as surface pretreatment to coat enamel and dentin with nanoparticles and explored the effect of enamel and dentin pretreatment with SNPs, ZNPs, and TNPs on the μ SBS of an etch-and-rinse adhesive. This pretreatment was aimed to benefit from the antibacterial properties of nanoparticles, and the probable effects of this pretreatment on the bond strength were evaluated in this study. The effect of dentin pretreatment with SNPs on the bond strength of adhesive systems was explored in a previous study. It was reported that SNPs had positive effects on the bond strength of adhesive systems with the best results achieved with Adper Single Bond and before acid etching. Moreover, no adverse effect was seen after application of 1 wt% SNPs on the color of composite resins.¹¹ Based on the findings of the mentioned previous study, the selected concentrations for the nanoparticles in the current study were 1 % to prevent the detrimental effect of these NPs on the color of composite resins. As with the previous study,¹⁵ visual observation did not reveal any color change after application of the nanoparticles with 1 wt% concentrations in this study.

Another nanoparticle which was used in this study was ZNP. Zinc oxide has a proper antibacterial activity which is improved by converting into nanoparticles because of the increased surface-to-volume ratio of the nanoparticles.³⁴ The antibacterial mechanism of ZNPs is related to modified cell membrane activity and oxidative stress resulting from the generation of active oxygen species such as H_2O_2 that inhibit bacterial growth.²¹ The leaching of Zn^{2+} into the growth media is another antibacterial mechanism that interferes with the bacterial metabolism by displacing Mg^{2+} .³⁵ Zinc oxide can also hinder the dental plaque acid production by inhibiting *Lactobacillus* and *Streptococcus mutans* although a higher concentration compared to NAPs was required for efficacy.^{18,19,33} Moreover, it has been reported that zinc has an inhibitory effect on the activity of matrix metalloproteinases (MMPs) which play roles in degradation of dentin collagen.³⁶ Osorio et al. showed a much longer effect on reducing collagen degradation in demineralized human dentin for zinc oxide (three weeks) as compared to that of chlorhexidine,

which was short-term. They also found that zinc had no adverse effect on bond strength to dentin which was per the result of the present study.³⁷ Zinc oxide also can stimulate a metabolic effect in hard tissue mineralization and inhibit dentin demineralization.^{38,39} Besides, a durable and strong bond at the resin/dentin interface was reported for zinc by decreasing collagen degeneration.³⁶ It was also shown that 1.23% and 13% concentrations of zinc oxide nanoparticles for bonding orthodontic brackets were able to decrease decalcification resulting from orthodontic treatment.⁴⁰ Additionally, composite resins containing silver nanoparticles or zinc oxide nanoparticles demonstrated higher antibacterial activity against *Streptococcus mutans* and *Lactobacillus* compared to the control group in a previous study.³⁴ In the present study, no adverse effects on μ SBS to dentin and enamel and composite resin color were observed after surface pretreatment with ZNPs. Therefore, enamel and dentin surface pretreatment with ZNPs can be suggested to benefit from the positive antibacterial effects of ZNPs.

Another nanoparticle which was used in this study was the TNP. The bactericidal mechanism of TiO₂ is the production of free radicals (HO• and O₂•-) which are strong oxidants with the capability to induce oxidative damage in the cell walls of microorganisms.⁴¹ Good anti-adhesive properties against *Streptococcus mutans* were also reported for TNPs in a previous study.⁴² It was shown that incorporating TiO₂ nanoparticles into composite resins conferred antibacterial properties to them. However, the mean shear bond strength of composite containing 10% NPs was lower than that of the control group.⁴³ Titanium dioxide (TiO₂) nanoparticles exhibit better antibacterial properties compared to chlorhexidine. Moreover, TNPs are suggested for preventing white spot formation because bacteria are less likely to develop resistance against TNPs.¹³ In the present study, enamel and dentin surfaces pretreated with TNPs presented the lowest values of μ SBS, albeit the differences were not significant to the control groups. This finding can be explained by the fact that because of the high surface energy and the resultant strong aggregation of the TNPs, dispersion of TNPs is difficult and this phenomenon directly affects their antimicrobial and physiochemical properties.⁴²

Based on the results of the present study, the dentin pretreatment with SNPs showed a statistically significant improvement in adhesive strength compared with the groups that use other nanoparticles as dentin pretreatment. The same result was observed for enamel, albeit the differences among different nanoparticles were not significant. This result can be attributed to the water-based character of SNPs that may provide an increase in the surface tension of the dentin substrate and help inadequate penetration of the adhesive system

through the etched dentin.⁴⁴ Another explanation for this finding may be due to the capability of silver to form silver compounds with chloride, phosphate, oxide, and proteins that have relatively low solubility within dentinal tubules which may lead to a durable gradual release of slight silver ions. This phenomenon may provide long-term antibacterial efficacy in the adhesive-tooth interface.⁴⁵ Moreover, higher dentin bond strength for SNPs compared to the ZNPs and TNPs might be attributed to the different chemical and colloidal stability of the NPs, charge of the NPs, morphologies, aggregation stability and surface-to-volume ratio of the NPs which leads to different interactions with enamel and dentin. Additionally, the differences in bond strength among the three groups pretreated with the three nanoparticles and the control group were not significant.

Thus, the behavior of different nanoparticles, their interaction with enamel and dentin and the adhesion protocols proposed by this study have to be further investigated, especially for their antibacterial and mechanical properties and toxicity, to be securely used in clinical practice. This study has some limitations. First, it was an *in vitro* study, and the results of the present study should be confirmed in future *in vivo* studies. Besides, only one adhesive system and three nanoparticles were used in this study, and we did not investigate the long-term bond strength properties, antibacterial and anti-caries effects of the nanoparticles. Therefore, further *in vitro* and *in vivo* studies are needed to investigate the effects of SNPs, TNPs and ZNPs pretreatment on enamel and dentin bond durability and the long-term antibacterial and anti-caries efficacy of these nanoparticles using various adhesive systems, composites, and glass ionomer cement. Moreover, the probable release of nanoparticles into oral cavity and saliva were not evaluated in this study, and they should be investigated in future.

CONCLUSION

Based on the result of this study, pretreatment with SNPs, TNPs, and ZNPs can be suggested to achieve potent antibacterial activities without compromising the bond strength. The best result was obtained for pretreatment with SNPs compared to pretreatment with TNPs or ZNPs in dentin and enamel, albeit the differences were not significant in the enamel groups.

CLINICAL SIGNIFICANCE

Effective antibacterial treatment prior to adhesive bonding application is desirable to provide successful restoration if it would not adversely affect the bond strength of the adhesive system. Nanoparticles can be applied to meet this goal.

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