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Janus Nanoparticles for Improved Dentin Bonding

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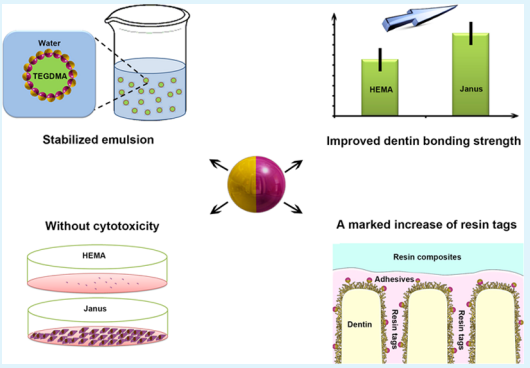
Supporting Information

ABSTRACT: The amphiphilic monomer 2-hydroxyethyl methacrylate (HEMA) is widely used in dental adhesives as a priming component, especially for dentin bonding. It behaves as a compatibilizer between hydrophilic and hydrophobic components and stabilizes the multicomponent adhesive system. However, there are several drawbacks associated with using HEMA, such as water retention within the adhesive layer, hydrolysis in oral environments, and cytotoxicity. These drawbacks lead to the failure of tooth restoration and represent a heavy medical burden. Thus, it is imperative to find a new compatibilizer to substitute for HEMA. Because of their superior compatibilization capabilities as functional solid surfactants, amphiphilic Janus particles are chosen as candidates for an alternative to HEMA in dental adhesives. Reactive amphiphilic Janus nanoparticles are synthesized by selectively etching and modifying at the interface of a Pickering emulsion. This approach could be extended to the synthesis of a series of other Janus nanoparticles. The Janus nanoparticles were verified to be better for the reduction of the phase separation and stabilization of dentin adhesives than HEMA. It is also demonstrated that these reactive Janus nanoparticles can strongly enhance the dentin bonding interface without cytotoxicity. It is clearly illustrated by this study that Janus nanoparticles may be promising materials to substitute for HEMA in dental adhesives.



KEYWORDS: *Janus nanoparticles, amphipathy, HEMA, dentin bonding, adhesive*

INTRODUCTION

Over the past two decades, Janus particles have aroused growing interest for their compositional and functional asymmetry.[1−5] As a result of their amphiphilic properties, Janus particles were first introduced as solid surfactants to stabilize the oil−water interface of emulsions. The advantages of the particle's Pickering effect and the surfactant's amphipathy are combined so that the emulsion is stabilized by Janus particles.[2,6] Weitz et al. demonstrated that amphiphilic snowman-like polystyrene (PS) dimer particles can assemble at liquid−liquid interfaces to stabilize emulsion drops. Janus particles can also pack closely at the interface to stabilize nonspherical drops.[7] More importantly, Janus particles have a well-defined orientation at the interface because of their amphiphilic properties.[8−10] This is essentially different from the homogeneous colloids rotating at the Pickering emulsion interface. In addition to their use in the oil−water interface of emulsion, Janus particles also can be used as compatibilizers to stabilize polymer blend interfaces. PS/poly(methyl methacrylate) (PMMA) Janus particles were used as stabilizers for the blend compatibilization of PS and PMMA polymers in a twin-screw minimixer.[11] The Janus particles could be located exclusively at the interface of the two polymer phases, despite the high temperature and shear conditions. The domain sizes of the dispersed phase decreased with increasing Janus particle content. Müller et al. demonstrated that by varying the loading of Janus particles based on PS-*b*-PB-*b*-PMMA triblock copolymers in conjunction with the mixing ratio of PS and PMMA, they can kinetically trap both bicontinuous and dispersed morphologies with tunable domain sizes in drop-cast films beginning as a single phase via solvent-induced demixing.[12] In addition, Janus particles with different compositions modified at different regions have been employed to stabilize rubber blends.[13] Therefore, Janus particles provide an interesting route for the nanoscopic engineering of polymer blend systems.

Dental caries is a chronic infectious disease and is essentially the localized chemical dissolution of the tooth surface caused

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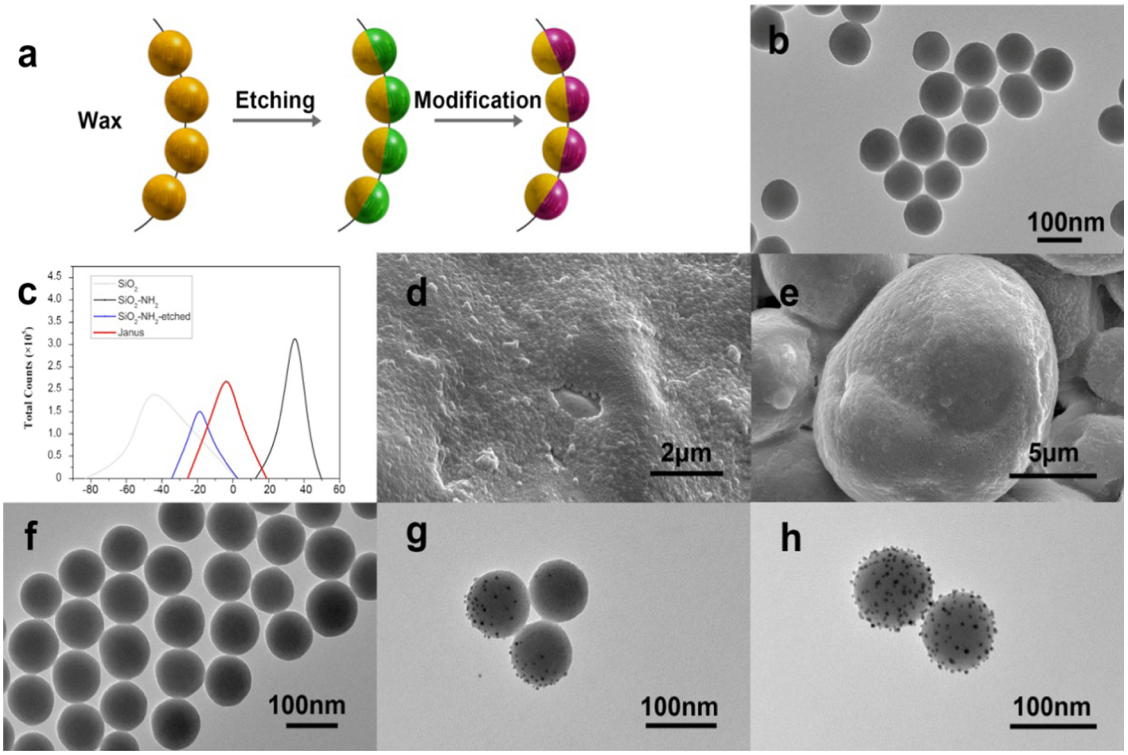

Figure 1. Representative images of the preparation process of Janus nanoparticles. (a) Schematic synthesis of Janus silica nanoparticles at the interface of a Pickering emulsion. (b) Transmission electron microscopy (TEM) images of amino-modified SiO_2 nanoparticles. γ-Aminopropyltriethoxysilane (APTES) is used to modify the surface of SiO_2 nanoparticles. After amino-modification, their morphology remains uniform. (c) Variation of ζ potential of different nanoparticles. A homogenous single layer of amino-modified SiO_2 nanoparticles is observed at the paraffin−water interface before (d) and after (e) the etching process. (f) TEM images of Janus nanoparticles. (g) TEM images of Janus nanoparticles labeled with Au nanoparticles; one side of the SiO_2 nanoparticles is labeled with Au nanoparticles, whereas the other side is not labeled. (h) TEM image of amino-modified SiO_2 nanoparticles labeled with Au nanoparticles. Different from the Janus nanoparticles, all of the sides were labeled.

by dental plaque. Dental caries is the most common dental disease in humans. If caries are not treated in a timely manner, they could turn to pulpitis and periapical periodontitis and even lead to tooth loss. These conditions cause considerable pain, suffering, and economic burden to the patient. In recent decades, polymer-based adhesive restoration in dentistry has brought significant changes to the treatment of caries. Dental adhesives are designed to provide strong coupling between resin composites and teeth. Teeth are special mineralized organs composed of enamel, dentin, cementum, and pulp, of which dentin is the main part. Unlike the enamel (mainly composed of hydroxyapatite), the dentin is a porous biologic composite made up of apatite crystal filler particles in a collagen matrix. Because of the moisture properties of the dentin surface, the widely used adhesive agents contain three categories of monomers according to the function, acidic monomers, hydrophilic monomers, and hydrophobic monomers, to etch and infiltrate dental tissues and then polymerize them with the bonding resin. The acidic monomers are mainly ionic resin monomers with acidic phosphate or carboxylic functional groups. The hydrophobic monomers are similar to those used in dental composite restoratives, thus ensuring that there will be strong interaction between the adhesive and the overlying composite. The widely commercially used hydrophilic monomer is 2-hydroxyethyl methacrylate (HEMA), and it serves as a bond-promoting agent.[14] HEMA behaves as a compatibilizer between the hydrophilic and hydrophobic components and stabilizes the multicomponent adhesive system. HEMA is broadly used in commercial dentin-bonding agents in amounts that vary from 35 to 55%.[15,16] However, there are several drawbacks associated with the use of HEMA, such as cytotoxicity,[17,18] water retention within the adhesive layer, and hydrolysis in oral environments.[19] These properties can damage the cells in the pulp through the dentin tubules, produce exposed dentin collagen fibers, weaken the mechanical strength of the adhesive, and damage the bonding stability.[20,21] Replacing failed restorations in the United States is estimated to cost over five billion dollars per year.[22] In our previous study, chlorhexidine-loaded amorphous calcium phosphate nanoparticles were prepared for inhibition of degradation and induction of mineralization of exposed type I collagen.[23] The goal was to protect the exposed dentin collagen fibrils and repair the bonding interface. However, the exposure of dentin collagen fibers in the bonding interface caused by using HEMA has not been resolved.

There exist HEMA-free adhesives in which a higher concentration of solvent (acetone) is added to omit HEMA. However, such adhesives are still far from perfect. The main drawback is that acetone is difficult to evaporate completely during the adhesion process and residual solvent may hamper the conversion of the monomers. In addition, phase separation could not be avoided because of the lack of compatibilizer and water droplets can occur in the adhesive interface.[24] Thus, it is imperative to find a new compatibilizer to substitute for HEMA. Because of their superior compatibilization capabilities as functional solid surfactants,[12,25,26] amphiphilic Janus particles are promising as an alternative to HEMA in dental adhesives.

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Herein, we fabricate Janus nanoparticles with different active groups on two sides via selective modification at a Pickering emulsion interface (Figure 1a). SiO_2 nanoparticles without cytotoxicity were used as the substrate materials. One side of the SiO_2 nanoparticles is modified with hydrophilic amino groups, and the other side is modified with hydrophobic acrylate groups. In this method, amino group-modified silica nanoparticles are used as emulsifiers to form a paraffin-in-water Pickering emulsion by arranging at the interface first. Then, the amino groups on the exterior side of SiO_2 nanoparticles are etched off and modified with acrylate groups to produce the Janus nanoparticles. When the Janus nanoparticles are used to enhance the interface between the teeth and filled resin, the amino groups react with the carboxyl groups on the surface of the etched dentin and the acrylate groups polymerize with bonding monomers.

MATERIALS AND METHODS

Preparation and Characterization of Janus Nanoparticles. *Materials.* γ-Aminopropyltriethoxysilane (APTES) and γ-mercaptopropyltrimethoxysilane (MPTMS) were purchased from Alfa Aesar. Paraffin wax (T_m: 52−54 °C) and all other reagents were purchased from Sinopharm Chemical Reagent Co., Ltd.

Preparation of Monodisperse SiO_2. A representative monodisperse SiO_2 colloid with a nanosized diameter was synthesized with the Stöber method. A mixture of 170.2 g of ethanol, 20 g of water, and 3.4 g of ammonia was stirred for 30 min. Then, 10.4 g of tetraethylorthosilicate was added into the mixture and the mixture was stirred for 24 h at 35 °C. The monodisperse SiO_2 was collected by centrifugation, washed with water, and lyophilized with a freeze-dryer (FD-1A-50, Boyikang, P. R. China).

Preparation of Amino-Modified Silica Nanoparticles (SiO_2-NH_2). Silica particles (1 g) were dispersed in 15 mL of ethanol, and then 1 g of APTES was added into the mixture. This mixture was stirred and heated to 76 °C under refluxing for over 24 h. The obtained amino-modified silica nanoparticles were washed with ethanol, collected by centrifugation, and lyophilized.

Preparation of Modified Silica Colloid-Stabilized Pickering Emulsion. A mixture of 0.1 g of amino-modified silica nanoparticles, 0.15 mL of 2 M HCl solution, and 1 g of paraffin was added to 15 g of water. The mixture was emulsified at 70 °C with a homogenizer at a speed of 18 000 rpm for 15 min to form a wax-in-water emulsion. After cooling to room temperature, the emulsion was filtered. The wax droplets were washed with water to remove the unattached silica nanoparticles and dried.

Synthesis of Janus Nonspherical Colloids by Etching the Exposed Side of the Silica Colloids and −C═C− Grafted at a Pickering Interface. A quantity of 0.1 g of the wax droplets was etched with 5 g of NH_4F solution (5 wt % in water) for 1 h, washed three times with tetrahydrofuran to remove the paraffin, and collected by centrifugation. The collected nanoparticles and 50 μL of MPTMS were ultrasonically dispersed in 3 mL of ethanol. The Janus nanoparticles were prepared after 24 h with a homogenizer and lyophilized.

Characterization. The structure and morphology of the samples were characterized using transmission electron microscopy (TEM) (JEM-1011, JEOL, Japan) and scanning electron microscopy (SEM) (S-4800, Hitachi, Japan). Chemical compositions were determined by energy dispersive X-ray spectroscopy (EDS) (S-4800, Hitachi, Japan). The Fourier transform infrared spectroscopy measurement was performed using a Bruker EQUINOX 55 spectrometer with the sample/KBr pressed pellets. The ζ potential was measured using a Zetasizer (Nano Series, Malvern Instruments, U.K.).

Cytotoxicity Evaluation of Nanoparticles. The CCK-8 test was used to evaluate the cytotoxicity of nanoparticles compared to that of HEMA. Mouse fibroblasts of the 3T3 immortalized cell line (2.5×10^3/well) were cultured in 96-well plates for 12 h. After incubation, the medium was removed and the cytotoxicity evaluation was performed. During the cytotoxicity assays, six groups were used: the negative control group, HEMA group, silica nanoparticle group, silica nanoparticles with amino-modification group (modified with APTES completely), silica nanoparticles with modification of carboxyl group (modified with MPTMS completely), and Janus nanoparticles group. The medicaments of each group were identical. After incubating the cells for 0, 1, 3, 5, and 7 days, cell viability was determined using Cell Counting Kit-8 (CCK-8; Dojindo, Kumamoto, Japan). Day 0 cells were those that were not incubated with the medium containing medicaments. In the experiment of cytotoxicity evaluation, the results of day 0 were used as the baseline. The cells were washed with phosphate-buffered saline twice and fresh culture medium (100 μL), and then the CCK-8 reagent (10 μL) was added to each well. After incubation for 2 h, the optical density of each well was measured using an Elx808 microplate reader (Bio-tek, Winooski, VT) at 450 nm with a reference wavelength of 630 nm.

Application of Janus Nanoparticles in Human Tooth Dentin Bonding. *Phase Separation Test.* The respective contents of triethylene glycol dimethacrylate (TEGDMA)/water/material (Janus nanoparticles or HEMA) in the mixture were 400 μL/2 mL/0.02 g. The material (3 mg, Janus nanoparticles or HEMA) was added to 100 μL of adhesive to observe the phase separation of the adhesives. This ratio was based on the minimum concentration for preventing the phase separation of the G-bond by a preliminary test. The same proportion was used for the following tests, including the μ-TBS test and the dentin bonding interface evaluation.

Microtensile Bond Strength (μ-TBS) Test and Dentin Bonding Interface Evaluation. Eighteen extracted sound human teeth were randomly divided into three groups: G-bond (group 1), G-bond + HEMA (group 2), and G-bond + Janus nanoparticles (group 3). Fifteen teeth were used to test the μ-TBS. Five teeth per group were randomly assigned to test the μ-TBS (Figure 3a,b). Tooth cusps were ground away under running water to expose a plane dentin surface. Then, the surfaces were coated with three categories of adhesives and the composite resins were filled to a height of 4 mm. The specimens were serially sectioned perpendicular to the cavity floor using a Leica SP1600 saw microtome, yielding stick-shaped specimens with a cross section of ∼1.0 × 1.0 mm^2. These stick-shaped specimens were mounted on a microtensile tester using a cyanoacrylate adhesive and stressed to failure in tension at 1 mm/min. The μ-TBS was expressed in MPa and calculated by dividing the fracture load (F) by the bond area (S): μ-TBS = F (N)/S (mm^2).

To further analyze the mechanism of the improved bonding strength of the Janus nanoparticle group, the dentin bonding interfaces of different groups were observed. The remaining three teeth were used (one tooth per group) in this test. The specimens were sectioned perpendicular to the cavity floor, yielding slab-shaped specimens (Figure 4a). After a slab-shaped specimen was prepared, it was subsequently pretreated with 6 mol/L hydrochloric acid and 5% sodium hypochlorite solutions, before carrying out SEM analysis.

RESULTS AND DISCUSSION

Monodisperse silica nanoparticles with a ∼70 nm diameter are first synthesized using the Stöber method (Figure S1, Supporting Information).[27] Then, APTES is used to modify the surface of the SiO_2 nanoparticles to achieve amino group-modified SiO_2 nanoparticles. The morphology of the nanoparticles remains uniform after the amino-modification (Figure 1b). The existence of elemental N in the EDX data proves that the amino groups are successfully modified onto the surface of the SiO_2 nanoparticles (Figure S2, Supporting Information). The ζ potential of the amino-modified SiO_2 nanoparticles changes from −46.1 (−Si−O^-) to +34.8 mV (−NH_4^+) (Figure 1c). The amino-modified SiO_2 nanoparticles are employed to stabilize the paraffin-in-water Pickering emulsion. A homogenous single layer of amino-modified SiO_2 nanoparticles is frozen at the paraffin−water interface after the temperature decreases to room temperature (Figure 1d). One part of the amino-modified SiO_2 nanoparticles is embedded into the

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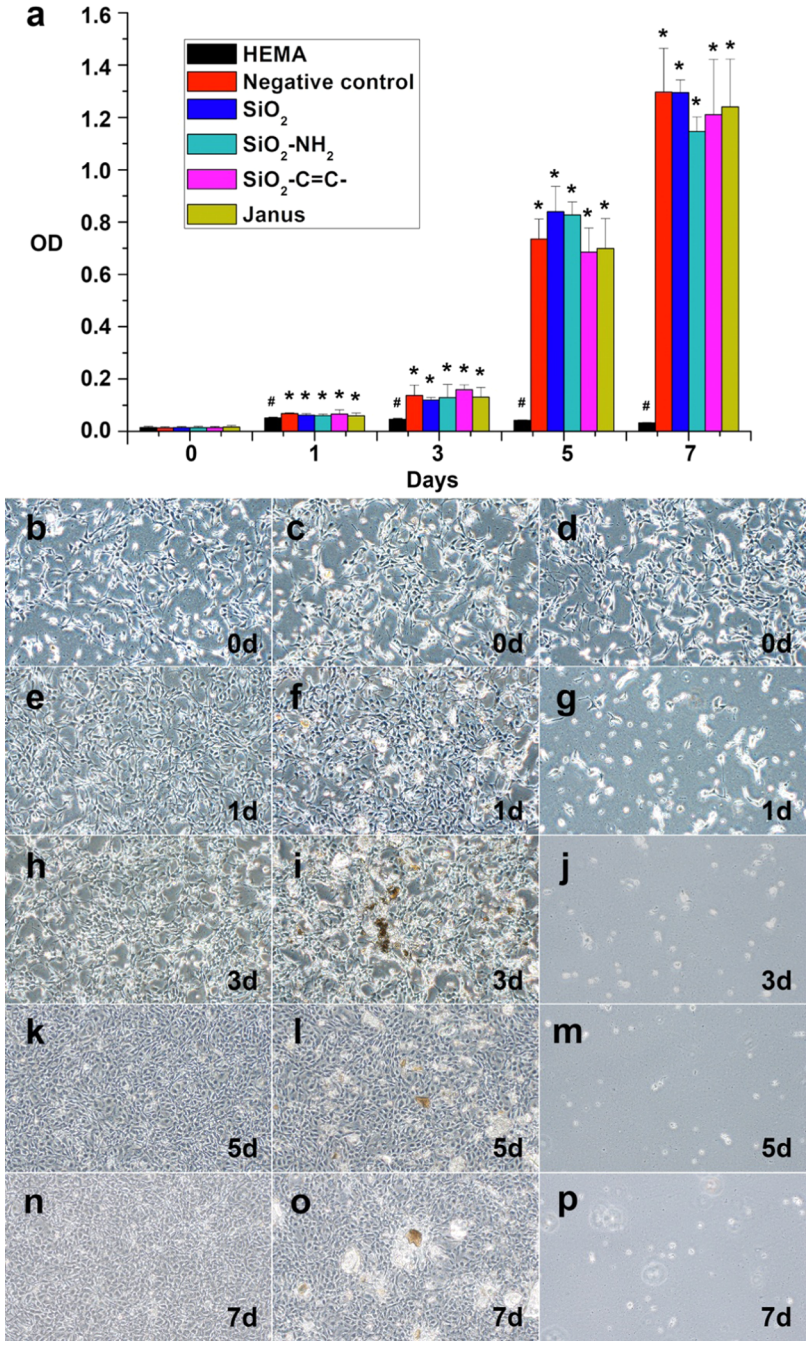

Figure 2. Cytotoxicity evaluation of the six groups, including the negative control, HEMA, silica nanoparticles, silica nanoparticles with amino-modification (modified with APTES completely), silica nanoparticles with modification of the acrylate groups (modified with MPTMS completely), and Janus nanoparticle groups. (a) CCK-8 test of HEMA and nanoparticles. (b, e, h, k, n) Cells of the negative control group observed with an inverted microscope. (c, f, i, l, o) Cells of the Janus nanoparticle group observed with an inverted microscope. (d, g, j, m, p) Cells of the HEMA group observed with an inverted microscope. The Janus nanoparticles could significantly reduce the cytotoxicity compared with HEMA.

paraffin droplets. Next, the externally exposed part of the amino-modified SiO_2 nanoparticles is etched with ammonium fluoride, whereas the other part is selectively protected in the paraffin. After the etching process, the single layer of the amino-modified SiO_2 nanoparticles remains on the surface of the paraffin droplets (Figure 1e). Because of the short etching time, the morphology of the as-etched SiO_2 nanoparticles remains intact (Figure S3, Supporting Information). However, the ζ potential of the as-etched SiO_2 nanoparticles changes from 34.8 ($-NH_4^+$) to −18.6 mV ($-NH_4^+$ and $Si-O^-$) (Figure 1c). Finally, MPTMS is used to modify the silicon (etched) side of the SiO_2 nanoparticles, whereas the amino side retains its spherical morphology (Figure 1f). The ζ potential of the as-formed SiO_2 nanoparticles changes to −3.25 mV because of the shielding of $Si-O^-$ (Figure 1c). The peaks at ∼3000 and 1700 cm^{-1} are assigned to the acrylate group of MPTMS, which is grafted onto the surface of the SiO_2 nanoparticles (Figure S4, Supporting Information). To approve the successfully selective modification, sodium citrate-modified Au nanoparticles are employed to selectively label the amino region of the SiO_2 nanoparticles. It is shown that one side of the SiO_2 nanoparticles is labeled with Au nanoparticles, whereas the

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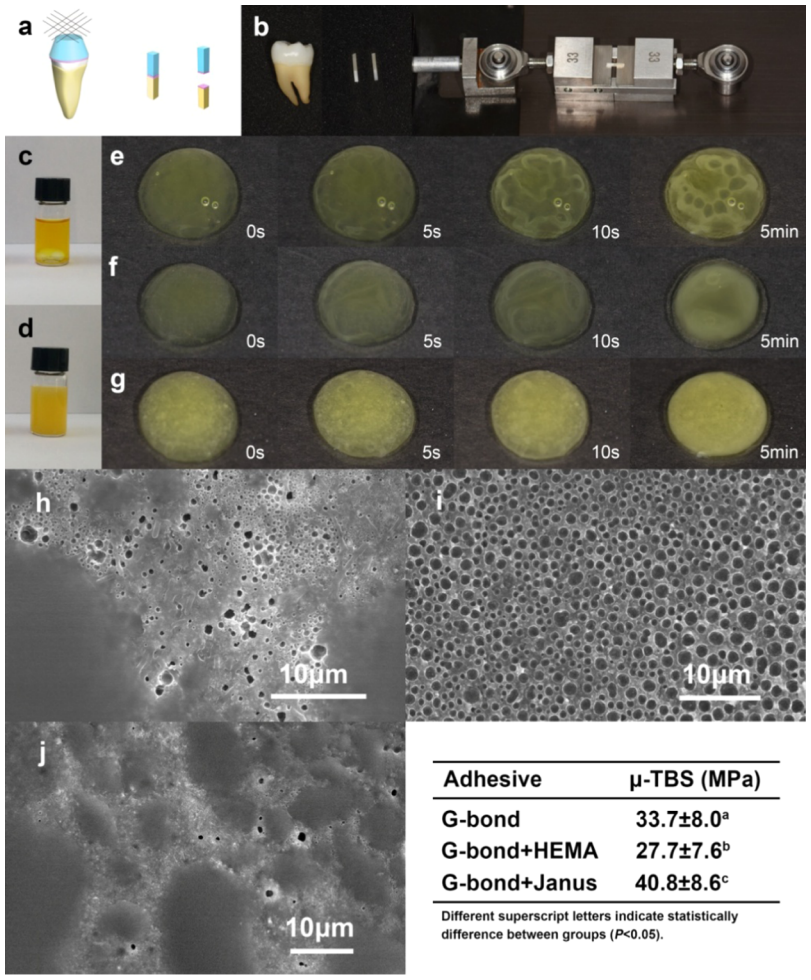

Adhesive	μ-TBS (MPa)
G-bond	33.7±8.0[a]
G-bond+HEMA	27.7±7.6[b]
G-bond+Janus	40.8±8.6[c]

Different superscript letters indicate statistically difference between groups (P<0.05).

Figure 3. Phase separation observation, the dentin bonding strength, and the observation of fracture bonding surfaces of different groups. The mold (a) and picture (b) of testing the microtensile bond strength. (c) Unstable emulsion stabilized by HEMA. (d) Emulsion stabilized by the Janus nanoparticles. (e) Digital images of the adhesive drops on a glass plate (0 s, 5 s, 10 s, and 5 min) of the G-bond group. (f) Digital images of the adhesive drops on a glass plate (0 s, 5 s, 10 s, and 5 min) of the G-bond + HEMA group. (g) Digital images of the adhesive drops on a glass plate (0 s, 5 s, 10 s, and 5 min) of the G-bond + Janus group. Phase separation of G-bond is inhibited with the Janus nanoparticles compared to that with HEMA. SEM images of the fracture surface of different groups: G-bond group (h), G-bond + HEMA group (i), and G-bond + Janus group (j).

other side is not labeled (Figure 1g). Alternatively, all of the surface of the amino-modified SiO_2 nanoparticles is labeled with sodium citrate-modified Au nanoparticles (Figure 1h). Thus, Janus nanoparticles with hydrophilic amino and hydrophobic acrylate groups on different sides of SiO_2 nanoparticles are achieved.

Regarding the biocompatibility of the nanoparticles, mouse fibroblasts of the 3T3 immortalized cell line were used in the CCK-8 test to evaluate the cytotoxicity. As shown in Figure 2a, there was no statistical difference in the cytotoxicity among the six groups on day 0 ($P > 0.05$). These results implied that the cells were distributed uniformly. Starting from day 1, the HEMA group showed significant cytotoxicity compared with the negative group ($P < 0.05$). Other groups, including the Janus nanoparticle group, showed no cytotoxicity compared with the negative group ($P > 0.05$). It is shown that the Janus nanoparticles could significantly reduce the cytotoxicity of HEMA. The cell growth patterns of the negative, HEMA, and Janus nanoparticle groups were observed with an inverted microscope and are shown in Figure 2b–p. The cell apoptosis was observed in the HEMA group from day 1, whereas the cells grew well in vitro in the Janus nanoparticle group and the negative group.

As a result of their amphiphilic nature, the Janus nanoparticles can serve as a solid surfactant to stabilize emulsions. Triethylene glycol dimethacrylate (TEGDMA, a representative ingredient of hydrophobic monomers) and water are used to form a TEGDMA-in-water emulsion stabilized with Janus nanoparticles. The as-formed emulsion is stable, whereas the demulsification occurs with the same quality of HEMA as the stabilizer (Figure 3c,d). It is shown that the Janus nanoparticles can enhance interfacial stability. G-bond is a representative HEMA-free dental adhesive prepared by adding substantial acetone. The phase separation between the water (hydrophilic) and oil (hydrophobic) phases usually reduces the bonding strength of the G-bond.[28] Both Janus nanoparticles and HEMA are employed to stabilize the phase structure of G-bond (Figure 3e–g). When HEMA acts as a stabilizer, phase separation occurs, which is similar to that without any stabilizer. However, phase separation is inhibited when the same amount of Janus nanoparticles is used. It is shown that the Janus nanoparticles can efficiently stabilize the interface between the hydrophilic components and hydrophobic components of G-bond to

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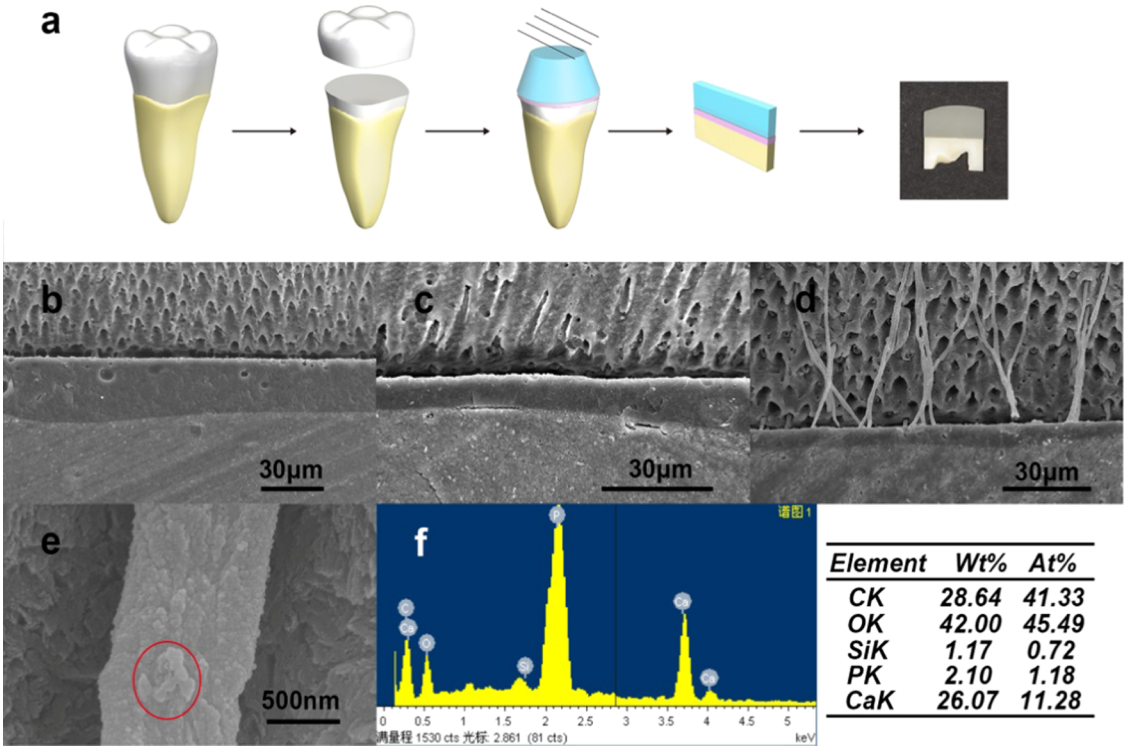

Figure 4. Dentin bonding interface of three groups. (a) Diagram of specimen preparation for the adhesive bonding interface. SEM images of the bonding interface of different groups: G-bond group (b), G-bond + HEMA group (c), and G-bond + Janus group (d). Magnified SEM image (e) and EDX spectrum (f) of Janus nanoparticles at the interfaces between the resin tags and dentin. The resin tags were significantly observed after adding Janus nanoparticles. The protruding structure with a size similar to that of the Janus nanoparticles could be observed on the surface of the resin tags.

achieve a stable phase structure due to the strengthened interfacial compatibility.

In addition to suppressing phase separation, these Janus nanoparticles can also enhance the bonding interface between the composite resin and dentin. The μ-TBS and dentin bonding interface were evaluated to verify the strengthened bonding interface. Animal experimental studies were not performed in this study. The structure of human tooth is different from that of a commonly used experimental animal. Because of the clinical needs for extraction of the impacted third molars of human beings, the human teeth could be used directly for dental restorative and bonding material research. Thus, this research model has been widely used in dental research and could be directly used to study the results of the teeth of human beings.

The adhesive fracture planes were observed with SEM (Figure 3h–j). The μ-TBS values are labeled in the bottom right corner table of Figure 3. The μ-TBS of group 3 (G-bond + Janus) was significantly higher than that of two other groups ($P < 0.05$). According to a previous study, the droplets of the G-bond adhesive interface should be ascribed to phase separation.[29] This is in accordance with a previous study. It is shown that although the water droplets were observed in the adhesive layer of all three groups the droplets decreased significantly after adding the Janus nanoparticles. This is because the phase separation of G-bond is reduced when Janus nanoparticles enhance the interface. However, adding HEMA with the same quality into the G-bond decreased the μ-TBS ($P < 0.05$) and increased the droplets on the interface significantly. According to previous studies, due to the lower molecular weight and strong hydrophilic character of HEMA, it functions as a semi-permeable membrane throughout the adhesive layer and allows for the transmission of small molecules through the adhesive layer, such as water.[30,31] The increased droplets of the group after adding HEMA results from water absorption from dentin through osmosis, which then decreases the bonding strength.

SEM images of the bonding interface of three groups are shown in Figure 4b–d. Compared with those in groups 1 and 2, the resin tags were significantly observed in group 3. The reason for this is that the additional carbonyl groups could be generated on the dentin due to the hydrolysis of certain peptide bonds after acid attack by the ionic resin monomers with acidic phosphate or carboxylic functional groups.[32] The amino-modification side of Janus nanoparticles could combine with the carbonyl groups of the dentin, and the other −C═C− side could combine with the adhesive monomers. The protruding structure with a size similar to that of the Janus nanoparticles could be observed on the surface of the resin tags (Figure 4e). The EDS results show that this is the Janus nanoparticles (Figure 4f). Thus, Janus nanoparticles efficiently enhance the interface bonding of tooth restoration.

CONCLUSIONS

In conclusion, we have developed a facile method to synthesize Janus nanoparticles via a selective etching/modification process at the interface of a Pickering emulsion. The Janus structure of SiO_2 nanoparticles was proved. One side is modified with amino groups, whereas the other side is modified with acrylate groups. This approach could be extended to the synthesis of a series of other Janus nanoparticles. The dentin bond strength could be improved by adding Janus nanoparticles as

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compatibilizers into adhesives without cytotoxicity. This may be due to the fact that the amino groups of the Janus nanoparticles could combine with the carboxyl groups of the etched dentin to increase the penetration ability of the adhesive to dentin (verified by increased resin tags). Meanwhile, phase separation of the adhesive could be reduced too. It could be deduced that Janus nanoparticles may be promising materials to substitute for HEMA in dental adhesives.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsami.7b19652.

Characterization results of prepared intermediate nanoparticles (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Takahara, Y. K.; Ikeda, S.; Ishino, S.; Tachi, K.; Ikeue, K.; Sakata, T.; Hasegawa, T.; Mori, H.; Matsumura, M.; Ohtani, B. Asymmetrically modified silica particles: a simple particulate surfactant for stabilization of oil droplets in water. *J. Am. Chem. Soc.* **2005**, *127*, 6271−6275.

(2) Glaser, N.; Adams, D. J.; Boker, A.; Krausch, G. Janus particles at liquid-liquid interfaces. *Langmuir* **2006**, *22*, 5227−5229.

(3) Choi, J.; Zhao, Y.; Zhang, D.; Chien, S.; Lo, Y. H. Patterned Fluorescent Particles as Nanoprobes for the Investigation of Molecular Interactions. *Nano Lett.* **2003**, *3*, 995−1000.

(4) Nisisako, T.; Torii, T.; Takahashi, T.; Takizawa, Y. Synthesis of Monodisperse Bicolored Janus Particles with Electrical Anisotropy Using a Microfluidic Co-Flow System. *Adv. Mater.* **2006**, *18*, 1152−1156.

(5) Howse, J. R.; Jones, R. A. L.; Ryan, A. J.; Gough, T.; Vafabakhsh, R.; Golestanian, R. Self-motile colloidal particles: from directed propulsion to random walk. *Phys. Rev. Lett.* **2007**, *99*, No. 048102.

(6) Aveyard, R.; Binks, B. P.; Clint, J. H. Emulsions stabilised solely by colloidal particles. *Adv. Colloid Interface Sci.* **2003**, *100−102*, 503−546.

(7) Kim, J. W.; Lee, D.; Shum, H. C.; Weitz, D. A. Colloid Surfactants for Emulsion Stabilization. *Adv. Mater.* **2008**, *20*, 3239−3243.

(8) Tang, C.; Zhang, C.; Liu, J.; Qu, X.; Li, J.; Yang, Z. Large Scale Synthesis of Janus Submicrometer Sized Colloids by Seeded Emulsion Polymerization. *Macromolecules* **2010**, *43*, 5114−5120.

(9) Liang, F.; Shen, K.; Qu, X.; Zhang, C.; Wang, Q.; Li, J.; Liu, J.; Yang, Z. Inorganic Janus nanosheets. *Angew. Chem., Int. Ed.* **2011**, *50*, 2379−2382.

(10) Sun, Y.; Liang, F.; Qu, X.; Wang, Q.; Yang, Z. Robust Reactive Janus Composite Particles of Snowman Shape. *Macromolecules* **2015**, *48*, 2715−2722.

(11) Walther, A.; Matussek, K.; Müller, A. H. Engineering nanostructured polymer blends with controlled nanoparticle location using Janus particles. *ACS Nano* **2008**, *2*, 1167−1178.

(12) Bryson, K. C.; Löbling, T. I.; Müller, A. H. E.; Russell, T. P.; Hayward, R. C. Using Janus Nanoparticles To Trap Polymer Blend Morphologies during Solvent-Evaporation-Induced Demixing. *Macromolecules* **2015**, *48*, 4220−4227.

(13) Nie, H.; Zhang, C.; Liu, Y.; He, A. Synthesis of Janus Rubber Hybrid Particles and Interfacial Behavior. *Macromolecules* **2016**, *49*, 2238−2244.

(14) Van Landuyt, K. L.; Snauwaert, J.; De Munck, J.; Peumans, M.; Yoshida, Y.; Poitevin, A.; Coutinho, E.; Suzuki, K.; Lambrechts, P.; Van Meerbeek, B. Systematic review of the chemical composition of contemporary dental adhesives. *Biomaterials* **2007**, *28*, 3757−3785.

(15) Hiraishi, N.; Breschi, L.; Prati, C.; Ferrari, M.; Tagami, J.; King, N. M. Technique sensitivity associated with air-drying of HEMA-free, single-bottle, one-step self-etch adhesives. *Dent. Mater.* **2007**, *23*, 498−505.

(16) Van Landuyt, K. L.; Snauwaert, J.; Munck, J. D.; Peumans, M.; Yoshida, Y.; Poitevin, A.; Coutinho, E.; Suzuki, K.; Lambrechts, P.; Meerbeek, B. V. Systematic review of the chemical composition of contemporary dental adhesives. *Biomaterials* **2007**, *28*, 3757−3785.

(17) Barbosa, M. O.; de Carvalho, R. V.; Demarco, F. F.; Ogliari, F. A.; Zanchi, C. H.; Piva, E.; da Silva, A. F. Experimental self-etching HEMA-free adhesive systems: cytotoxicity and degree of conversion. *J. Mater. Sci.: Mater. Med.* **2015**, *26*, No. 5370.

(18) Soares, D. G.; Brito, C. A.; Tavares da Silva, R. H.; Ribeiro, A. P.; Hebling, J.; de Souza Costa, C. A. Cytocompatibility of HEMA-free resin-based luting cements according to application protocols on dentine surfaces. *Int. Endod. J.* **2016**, *49*, 551−560.

(19) Ferracane, J. L. Hygroscopic and hydrolytic effects in dental polymer networks. *Dent. Mater.* **2006**, *22*, 211−222.

(20) Collares, F. M.; Ogliari, F. A.; Zanchi, C. H.; Petzhold, C. L.; Piva, E.; Samuel, S. M. W. Influence of 2-hydroxyethyl methacrylate concentrationon polymer network of adhesive resin. *J. Adhes. Dent.* **2011**, *13*, 125−129.

(21) Carrilho, M. R.; Carvalho, R. M.; Tay, F. R.; Yiu, C.; Pashley, D. H. Durability of resin-dentin bonds related to water and oil storage. *Am. J. Dent.* **2005**, *18*, 315−319.

(22) Jokstad, A.; Bayne, S.; Blunck, U.; Tyas, M.; Wilson, N. Quality of Dental Restorations. FDI Commission Project 2−95. *Int. Dent. J.* **2001**, *51*, 117−158.

(23) Cai, X.; Han, B.; Liu, Y.; Tian, F.; Liang, F.; Wang, X. Chlorhexidine-Loaded Amorphous Calcium Phosphate Nanoparticles for Inhibiting Degradation and Inducing Mineralization of Type I Collagen. *ACS Appl. Mater. Interfaces* **2017**, *9*, 12949−12958.

(24) Van Landuyt, K. L.; Snauwaert, J.; De Munck, J.; Coutinho, E.; Poitevin, A.; Yoshida, Y.; Suzuki, K.; Lambrechts, P.; Van Meerbeek, B. Origin of interfacial droplets with one-step adhesives. *J. Dent. Res.* **2007**, *86*, 739−744.

(25) Virgilio, N.; Favis, B. D. Self-Assembly of Janus Composite Droplets at the Interface in Quaternary Immiscible Polymer Blends. *Macromolecules* **2011**, *44*, 5850−5856.

(26) Bahrami, R.; Löbling, T. I.; Gröschel, A. H.; Schmalz, H.; Müller, A. H. E.; Altstädt, V. The Impact of Janus Nanoparticles on the Compatibilization of Immiscible Polymer Blends under Technologically Relevant Conditions. *ACS Nano* **2014**, *8*, 10048−10056.

(27) Stöber, W.; Fink, A.; Bohn, E. Controlled growth of monodisperse silica spheres in the micron size range. *J. Colloid Interface Sci.* **1968**, *26*, 62−69.

(28) Van Landuyt, K. L.; Mine, A.; De Munck, J.; Jaecques, S.; Peumans, M.; Lambrechts, P.; Van Meerbeek, B. Are one-step adhesives easier to use and better performing? Multifactorial

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ACS Appl. Mater. Interfaces 2018, 10, 8519−8526

assessment of contemporary one-step self-etching adhesives. *J. Adhes. Dent.* **2009**, *11*, 175−190.
(29) Van Landuyt, K. L.; Snauwaert, J.; De Munck, J.; Coutinho, E.; Poitevin, A.; Yoshida, Y.; Suzuki, K.; Lambrechts, P.; Van Meerbeek, B. Origin of interfacial droplets with one-step adhesives. *J. Dent. Res.* **2007**, *86*, 739−744.
(30) Chersoni, S.; Suppa, P.; Grandini, S.; Goracci, C.; Monticelli, F.; Yiu, C.; Huang, C.; Prati, C.; Breschi, L.; Ferrari, M.; Pashley, D. H.; Tay, F. R. In vivo and in vitro permeability of one-step self-etch adhesives. *J. Dent. Res.* **2004**, *83*, 459−464.
(31) Tay, F. R.; Pashley, D. H.; Suh, B. I.; Carvalho, R. M.; Itthagarun, A. Single-step adhesives are permeable membranes. *J. Dent.* **2002**, *30*, 371−382.
(32) Di Renzo, M.; Ellis, T. H.; Sacher, E.; Stangel, I. A photoacoustic FTIRS study of the chemical modifications of human dentin surfaces: I. Demineralization. *Biomaterials* **2001**, *22*, 787−792.

DOI: 10.1021/acsami.7b19652
ACS Appl. Mater. Interfaces 2018, 10, 8519−8526