Bioinspired dopamine-conjugated polyaspartamide as a novel and versatile adhesive material

B. Wang, Y. S. Jeon, S. H. Bhang, J-H. Kim*

Department of Chemical Engineering, Sungkyunkwan University, 16419 Suwon, South Korea

Received 13 December 2016; accepted in revised form 23 February 2017

Abstract. Biomimetic dopamine-conjugated polyaspartamides as novel adhesive materials were synthesized and characterized. These modified polyaspartamides contain three different groups combined with dopamine (DOPA), i.e., γ -amino butyric acid (GABA), ethanolamine (EA) and octylamine (OA), which are referred to as PolyAspAm (DOPA/GABA), PolyAspAm(DOPA/EA) and PolyAspAm(DOPA/OA), respectively. These three water-swollen polymer glues show good adhesion (0.1~0.4 MPa) with various daily-life materials (aluminum foil, glass and paper) as well as some plastic substrates (PET and PMMA). Compared to the polymers with more hydrophilic groups (GABA and EA), the polymer glue with the hydrophobic alkyl group (OA) exhibited higher adhesive strength values on most substrates. In addition, when applied to biological porcine skin, these glues demonstrated adhesion of values of 15~20 kPa with EA- and OA-conjugated polymers. These results suggest the great potential of dopamine-modified polyaspartamides as versatile and efficient polymeric glues for industrial and biomedical applications.

Keywords: adhesion, polymer glue, biomimetic, polyaspartamide, dopamine

1. Introduction

Biomimetic materials, which are designed to mimic biological compounds, have been extensively reviewed as novel materials for various applications due to their specific functionality and desirable properties [1–3]. Bioadhesive reagents play an important role in many life systems, and the application potential of these kinds of adhesives has attracted a lot of research [4, 5]. However, it is difficult to synthesize bioadhesives that can be applied in aqueous environments that are resistant to water and wave impacts; this is due to the existence of a weak boundary layer of water at the interfaces between the adherend and substrates or to the swelling of the adhesive by water absorption [6]. Marine mussels (*mytilus edulis*), such as the blue mussel, attach to a variety of surfaces in aqueous environments through the use of a natural adhesive that is incredibly strong and can form durable bonds to glass, plastic, wood, concrete, and Teflon

[1, 7–9]. Marine mussels withstand high-energy wave impacts in rocky seashore habitats by fastening tightly to surfaces with tough and self-healing proteinaceous fibers, called byssal threads, composed of 25–30 different types of underwater mussel adhesive proteins (UMAPs) [10–13]. 3,4-Dihydroxy-phenylalanine (DOPA) residues, which are modified amino acids, have catecholic functionality and can be found in UMAPs. The catechol groups of dopamine can strongly interact with a variety of organic/inorganic substrates via coordination, covalent bonds, π - π stacking, electrostatic forces, and hydrogen bonding, which allows mussels to attach to various surfaces such as glass, plastic, wood and metals in an aqueous environment [11–17].

In 1981, Waite and Tanzer determined that catechols were responsible for the adhesion of mussels in inhospitable regions under very harsh and wet conditions [18]. Since this discovery, researchers have focused

*Corresponding author, e-mail: kimjh@skku.edu
© BME-PT

on incorporating DOPA into polymers for a variety of adhesive applications [18–21]. Stepuk and collaborators introduced a mussel-inspired synthetic adhesive based on the copolymer of dopamine methacrylamide (DMA) with methyl methacrylate (MMA), which is a copolymer with catechol functionality [22]. When this coating was subjected to a macroscopic load, effective transfers of mechanical stress from the metal matrix to the polymer cement improved the strength of conventional PMMA cements bonded to titanium and aluminum. Matos-Pérez *et al.* [23] presented a structure-property study on the simplest mimic of mussel adhesive proteins. They synthesized a series of poly(3,4-dihydroxystyrene-co-styrene) by varying the 3,4-dihydroxystyrene content to test the effect of this content on the bulk adhesion of the material on aluminum substrates. Their results showed that increasing the catechol content up to 33% led to an increase in the lap shear adhesion. In order to explore the role of charge on adhesion, White and Wilker developed a family of biomimetic copolymers by incorporating both DOPA and ammonium groups, which can give cationic charges [24]. The bulk adhesion of this dried copolymer was found to be similar to that of commercial glue. While underwater adhesion was lower than dry adhesion it was still superior to three popular commercial products. In 1987, Waite revealed the effect of water on adhesion. He proposed four pathways to explain how the presence of water affected the adhesion properties. Mussels can achieve remarkable adhesion to various surfaces underwater using their byssal threads, which are heavily decorated with DOPA. Researchers have been looking for inspiration from mussels to produce bio-inspired wet adhesives for application as biomedical adhesives [3, 25–27]. Chung and Grubbs described newly designed DOPA-containing terpolymer adhesives that were prepared by the polymerization of three vinyl monomers: acrylic acid (AA), acrylic acid *N*-hydroxysuccinimide ester (AANHS), and *N*-methacryloyl-3,4-dihydroxyl-*L*-phenylalanine (MDOPA), and suggested that these materials could represent clinically-useful biomedical adhesives [28]. When the DOPA moiety was introduced into the adhesives, the adhesion strength increased by 190% during lap shear tests on wet porcine skin. Jo and Sohn copied the mechanism of underwater medical adhesives by blending modified DOPA and a triblock

copolymer (PEO-PPO-PEO) to synthesize the triblock copolymer poly(dopamine methacrylamide-co-methoxyethyl acrylate-co-2-ethylcyano acrylate) [poly(DMA-co-MEA-co-ECA), PDMC] [29]. This novel synthetic copolymer adhesive can be applied to repair wet living tissues or bone with maximum stress and modulus values of 165 kPa and 33 MPa, respectively, in the wet state.

Polyaspartamides are promising water-soluble, non-toxic, nonantigenic, and biodegradable polymers that can be obtained from the aminolysis of polysuccinimide (PSI), which is the thermal polycondensation product of the aspartic acid monomer [30–33]. In this work, we present a mussel-inspired synthetic adhesive based on dopamine-containing polyaspartamide derivatives that is applicable to various kinds of substrates such as paper, plastic, glass, and metals. In addition, these polymer glues showed adhesion properties when applied to biological porcine skin. Hence, this novel and biocompatible polymer glue system has the potential to be used as a medical bioadhesive, sealant and industrial glue.

2. Experimental

2.1. Materials

L-aspartic acid (98%+), orthophosphoric acid (98%), *N,N*-dimethylformamide (99.8% anhydrous, DMF), γ -aminobutyric acid (99%+), chlorotrimethylsilane (99%+), dopamine hydrochloride (DOP), ethanolamine (99%, EA), octylamine (99.5%+, OA), dibutylamine (99.5%+), sodium hydrosulfite (ca. 85%), acetic acid (99%+), and methanol (99.9%+) were purchased from Sigma-Aldrich. Acetone and ethyl ether were obtained from DaeJung Chemical Co. (Siheung, Korea). All of the other chemicals that were purchased were of sufficient quality and were used as.

2.2. Synthesis of polysuccinimide (PSI)

PSI was prepared and purified using previously reported procedures [30, 34]. L-aspartic acid (30 g) and o-phosphoric acid (30 g) (50:50 wt. ratio) were put into a round-bottom flask and mixed at room temperature. The mixture was heated slowly from room temperature to 180 °C under reduced pressure for about 30 min and then maintained at 180 °C for 4.5 h. The reaction mixture was then cooled and DMF was added to dissolve the product. The resulting solution was precipitated in excess water and the precipitate

was washed several times with water to remove residual phosphoric acid until the solution reached pH 7. The product was then dried at 70 °C under vacuum for 3 d to obtain PSI in the form of an off-white powder. The molecular weight was estimated to be approximately 75 000 Da, as calculated from an empirical equation relating the solution viscosity to the molecular weight.

2.3. Synthesis of polyaspartamide derivative PolyAspAm(DOPA/GABA)

First, 0.97 g of PSI (corresponding to 0.01 mol of succinimide unit) was dissolved in 20 mL of DMF. Then, 6.5 mmol of γ -aminobutyric methyl ester hydrochlorides (GABAME), an ester derivative of γ -aminobutyric acid (GABA) as the synthesis shown in our previous report [35], and 6.5 mmol of dibutylamine (DBA) were dissolved in 20 mL of DMF. This solution was then added to the PSI solution under vigorous stirring at room temperature. After reaction for 5 days, 0.01 mol of DOP and 0.005 mol of DBA were added. The reaction was carried out under a nitrogen atmosphere in the presence of 0.05 g of sodium hydrosulfite. The reaction mixture was placed in an 80 °C water bath and stirred for 24 h. The resulting mixture was precipitated in 300 mL of cold acetone, from which the product, PolyAspAm(DOPA/GABA), was separated by filtration. The product was dispersed in a pH 10 solution of sodium hydroxide in distilled water; additional sodium hydroxide solution was dropped into the dispersion to maintain its pH at about 10. The mixture was stirred overnight and then hydrochloric acid was dropped into the solution until its pH was stabilized at pH 4.0. The resulting solution was filtered, dialyzed, and lyophilized to obtain a solid polymer (2.11 g).

2.4. Synthesis of polyaspartamide derivative PolyAspAm(DOPA/EA)

First, 0.97 g of PSI (corresponding to 0.01 mol of succinimide units) was dissolved in 20 mL of DMF. Then, DOP (100 mol%, based on the succinimide units) and 3.6 mL of dibutylamine were added. The reaction was carried out under a nitrogen atmosphere in the presence of 0.05 g of sodium hydrosulfite. The reaction mixture was placed in an 80 °C water bath and stirred for 24 h. Subsequently, 50 mol% of EA was added slowly to the reaction mixture and stirred

at room temperature for another 24 h. The resulting mixture was precipitated in 300 mL of cold acetone. The filtered product was dried in oven at 40 °C for 3 days to obtain the final product (1.93 g).

2.5. Synthesis of polyaspartamide derivative PolyAspAm(DOPA/OA)

First, 0.97 g of PSI (corresponding to 0.01 mol of succinimide units) was dissolved in 20 mL of DMF. Then, DOP (100 mol% based on the succinimide units) and 3.6 mL of dibutylamine were added. The reaction was carried out under a nitrogen atmosphere in the presence of 0.05 g of sodium hydrosulfite. The reaction mixture was placed in an 80 °C water bath and stirred for 24 h. Subsequently, 50 mol% OA was added to the flask, which was then heated at 70 °C and stirred for 6 h. The resulting mixture was precipitated in 300 mL of cold acetone. The filtered product was washed and dried at 40 °C under vacuum for 3 days to obtain the final product (2.15 g).

2.6. Characterization and measurements

NMR: ^1H NMR spectra of samples were acquired using a Unity Inova-500 (Varian, Palo Alto, CA, USA) spectrometer.

Fourier-transform infrared spectroscopy

The structures of PolyAspAm derivatives were analyzed by means of Fourier transform infrared spectroscopy (FT-IR, Perkin Elmer System 2000 FT-IR).

Measurement of water absorption capacity

The water absorbency and swelling rate were measured in DI water. A certain amount of dry polymer powder (W_d) was weighed and then placed in distilled water until near-equilibrium swelling was obtained. The weight of the swollen polymer was subtracted to obtain the pure weight of the swollen gel (W_s) resulting from the dry polymer. The swelling percentage was simply calculated as shown by Equation (1):

$$\text{Water absorption} = \frac{(W_s - W_d)}{W_d} \quad (1)$$

Bulk adhesion tests

Lap shear testing was performed on a UTM (QC-508E, Comotech, Taiwan) with a 100 N load cell at

a speed of $15 \text{ mm} \cdot \text{min}^{-1}$. Adhesion forces, expressed in Pascals [Pa], were obtained by dividing the shear force (in Newtons) by the adherend overlap area. Each DOPA-containing polyaspartamide was mixed with the same weight of DI water (for example 0.5 g of polymer in 0.5 mL of water) and the resulting viscous paste was spread on the substrate to cover the overlapping area using substrates of the same size (length: 7.5 cm, adhesion area: 2.0 cm in length $\times$ 2.5 cm in width).

Porcine skin preparation and test

Porcine skin samples were cut into rectangular pieces (7.5 cm in length $\times$ 2.0 cm in width) and washed with a sodium chloride aqueous solution. These were then soaked for 12 h in a PBS buffer solution (pH = 7.4) [36]. For the adhesion test, polyaspartamide glues were spread on two pieces (2.0 cm $\times$ 1.5 cm cross area) of the porcine skin surface. The adhesion test was carried out as described above.

In vitro cytotoxicity test

The cytotoxicity of polyaspartamide derivatives were measured by an MTT assay in vitro. 293T cells in 2 mL media were settled in 6-well plate, and cultured for 24 h at 37°C and 5% CO_2 atmosphere. Media was changed with 2 mL fresh media, and then three different polymers were placed in the well with a certain concentration (0.01, 0.03, 0.05, 0.1, and $0.2 \text{ mg} \cdot \text{mL}^{-1}$). In case of PolyAspAm(DOPA/OA) with poor solubility, a well dispersion was obtained by adding 5% DMSO in the cell culture medium. The cell and polymer were further incubated for 24 h. Then, these mixtures were removed from the well. Afterward, 100 μL of MTT solution (5 mg/mL) was added and the plate was incubated at 37°C for another 3 h. After removing the medium, 1.6 mL of DMSO was added to each well and incubated at 60°C for 1 h. 200 μL of cell sample was transferred into 96 wells plate and the absorbance was checked via microplate reader at a wavelength of 570 nm.

3. Results and discussion

3.1. Synthesis and characterization of polyaspartamide derivatives

As shown in Figure 1, polyaspartamide derivatives were synthesized from PSI by means of successive aminolysis reactions using quantitative amounts of

Figure 1. Synthesis of dopamine-conjugated polyaspartamides

γ -aminobutyric acid (GABA), ethanolamine (EA), and octylamine (OA) and the reaction yield of three derivatives were 80~85%. The structures and compositions of PSI and the polyaspartamide derivatives were confirmed by ^1H NMR spectroscopy using $\text{DMSO}-d_6$ as the solvent (Figure 2). The methine proton (at 5.3 ppm) of the initial succinimide ring disappeared completely during the series of aminolysis reactions, suggesting a quantitative ring opening to produce the PolyAspAm derivatives. For these three polymers, the aromatic protons of the dopamine phenyl groups were observed at around 6.5 ppm (three peaks). In the case of PolyAspAm(DOPA/GABA), two peaks at 1.6 and 2.2 ppm were assigned

Figure 2. ^1H NMR spectra of (A): PSI, (B): PolyAspAm(DOPA/OA), (C): PolyAspAm(DOPA/EA) and (D): PolyAspAm(DOPA/GABA)

Table 1. Amount of each pendant group in polyaspartamide derivatives determined from ^1H NMR analysis

PolyAspAm(DOPA/GABA)	Content [mol%]	PolyAspAm(DOPA/EA)	Content [mol%]	PolyAspAm(DOPA/OA)	Content [mol%]
DOPA	49	DOPA	47	DOPA	52
GABA	51	EA	53	OA	48

Figure 3. FTIR spectra of PSI and the three different polyaspartamides

to the characteristic methylene protons of the GABA pendant. Alternatively, in PolyAspAm (DOPA/OA), the peaks at 0.8, 1.1 and 1.2 ppm were assigned to the characteristic methylene protons of the octyl pendant. Table 1 lists the compositions of the polyaspartamide derivative copolymers. Figure 3 shows the FT-IR transmittance spectra of polysuccinimide (PSI), PolyAspAm(DOPA/GABA), PolyAspAm(DOPA/EA) and PolyAspAm(DOPA/OA). PSI showed a characteristic band at 1706.8 cm^{-1} , which was attributed to the absorption of the imide ring. For the three polyaspartamide derivative polymers, the broad bands around 3294 cm^{-1} were assigned to $-\text{OH}$ and $-\text{NH}$ groups of the polymers. The peaks related to succinimide disappeared and new peaks related to amide I and amide II bands appeared at around 1645 and 1518 cm^{-1} . The absorption bands around 1382 and 1280 cm^{-1} could be assigned to the phenolic $\text{C}-\text{O}-\text{H}$ of the catechol group in dopamine. In addition, the spectrum of PolyAspAm(DOPA/OA) showed two characteristic bands at 2960.1 and 2931.1 cm^{-1} , which were attributed to the absorption of alkyl $-\text{CH}_3$ and $-\text{CH}_2$. In the case of PolyAspAm(DOPA/GABA), the characteristic band at 1721.7 cm^{-1} is assignable to $\text{C}=\text{O}$ carbonyl stretching. As a result, NMR and FT-IR analyses confirmed the successful synthesis of the polyaspartamide derivative polymers.

3.2. Water absorption capacities of polyaspartamide derivatives

The water absorption capacities of the three different polymers, PolyAspAm(DOPA/GABA), PolyAspAm(DOPA/EA) and PolyAspAm(DOPA/OA), were measured. Figure 4 shows the water absorption curves for the samples in deionized (DI) water. In the case of PolyAspAm(DOPA/OA), which contains hydrophobic octyl (C8) groups, the initial rapid swelling appeared to reach equilibrium within several hours, and the water absorption value was approximately 1. The water absorption capacity was found to vary depending on the functional group that was introduced. When the hydrophilic GABA moiety was introduced onto polyaspartamide, the swelling of PolyAspAm(DOPA/GABA) occurred over a longer period of time and exhibited a much higher degree of swelling with a water absorption value of approximately 6.5. The water absorption capacity of PolyAspAm(DOPA/EA) was about 5, which was slightly lower than that of PolyAspAm(DOPA/GABA). This suggests that the $-\text{OH}$ group gives highly polar and hydrophilic character but has a smaller effect compared to $-\text{COOH}$; this was expected. The overall relative water absorption capacity among these three polyaspartamide polymers was in the order of PolyAspAm(DOPA/OA) < PolyAspAm(DOPA/EA) < PolyAspAm(DOPA/GABA).

Figure 4. Water absorption of polyaspartamide derivatives in DI water

Figure 5. Image of dopamine-conjugated polyaspartamide derivative glue

3.3. Adhesion properties of polyaspartamide derivative glues

The preparation of polyaspartamide glue was demonstrated using the PolyAspAm(DOPA/EA) polymer as one sample. Typically, 0.05 g of a PolyAspAm(DOPA/EA) un-adhesive powder was mixed with 0.05 mL of DI water to form a very sticky paste-like glue, as shown in Figure 5. Because the strong hydrogen-bond formation in the polymer can induce intensive aggregation and chain entanglement, limiting the solubility in water, the polymer did not dissolve in water even after prolonged exposure [28].

To quantify the adhesion behavior, a widely-used lap shear test method was employed. Of the many parameters affecting adhesion, the substrate onto which a material is bonded is one of the most important [21]. Figures 6a and 6b show the preparation of the sample for lap shear testing. Figure 6c demonstrates the adhesion and adhesive power on aluminum adherend using polyaspartamide glue. When a 100 g weight was suspended to the lower aluminum substrate, there was no rupture between the two substrates, as can be observed in the actual image.

In general, substrates can be divided into low-surface-energy plastics and high-surface-energy metals. It is typically easier to obtain strong adhesion to a high-energy, rough surface [21]. Figure 7 shows the bulk adhesive strengths for three different adherends that are conventionally used as daily-life materials (aluminum foil, glass and paper). In the case of aluminum foil, the bulk shear adhesive strength values were 0.10 ± 0.006 MPa for PolyAspAm(DOPA/GABA), 0.19 ± 0.025 MPa for PolyAspAm(DOPA/EA), and 0.28 ± 0.015 MPa for PolyAspAm(DOPA/OA). Interestingly, the PolyAspAm(DOPA/OA) polymer, which has hydrophobic alkyl pendants, exhibited much higher adhesion strengths compared to the other two polymers. The explanation for this result is not simple,

Figure 6. Schematic illustration of bulk shear strength test (a, b), and an actual image of lap shear test using aluminum foil substrate (c)

but a decrease in the weak boundary layer of water at the interfaces between the adhesive and substrate presumably results in enhanced adhesive strength. Conversely, the polymer conjugated with hydrophilic GABA showed the lowest adhesive strength. In the same manner as the aluminum foil, the glass and paper adherends also exhibited the highest shear adhesive strengths for the PolyAspAm(DOPA/OA) glue with values of 0.39 ± 0.024 MPa and 0.40 ± 0.006 MPa, respectively. For the paper with surface roughness, it showed highest shear adhesive strength values, where the failure occurred at the inner part of the paper and not at the interface. This suggests that the real adhesive strength can be much higher than the measured strength value.

From the test on the water absorption capacity as described above, the overall relative hydrophilicity

Figure 7. Lap shear strength test of polyaspartamide derivative glues on daily-life materials (aluminum foil, glass, and paper)

among the three polyaspartamide derivatives polymers came out in the order of PolyAspAm(DOPA/OA) < PolyAspAm(DOPA/EA) < PolyAspAm(DOPA/GABA). Comparing the bulk adhesive strengths for three different adherends which are conventional daily-life materials and plastics, PolyAspAm(DOPA/OA) glue exhibited higher adhesive strength values for most of the substrates than those of PolyAspAm(DOPA/EA > PolyAspAm(DOPA/GABA), suggesting that the lower water absorption capacity (or hydrophilicity) of polymer glue show the higher adhesive strength values. To summarize, above adhesive property results indicate that dopamine-containing polyaspartamide derivative glues can act efficiently as adhesives for various daily-life substrates. The strong adhesive strength can be ascribed to the adhesive function of dopamine, forming strong hydrogen and coordination bonds that combine with the hydrophobic interaction to enhance the cohesion of polyaspartamide glues.

Obtaining strong adhesion between plastics is a challenging task. In Figure 8, the three polyaspartamide glues showed relatively strong adhesion for three arbitrarily chosen plastics. For the PET and PMMA substrates, shear adhesive strength values of 0.22 ± 0.032 and 0.31 ± 0.019 MPa for PolyAspAm(DOPA/OA), 0.15 ± 0.011 and 0.17 ± 0.019 MPa for PolyAspAm(DOPA/EA), and 0.09 and 0.06 MPa for PolyAspAm(DOPA/GABA) were obtained, respectively. The relative adhesive strengths among these three different polyaspartamide glues were in the order of PolyAspAm(DOPA/OA) > PolyAspAm(DOPA/EA) > PolyAspAm(DOPA/GABA), which was the same order

Figure 8. Lap shear strength test of polyaspartamide derivative glues on several plastic substrates (PET, PMMA, and PS)

Figure 9. Image depicting the measurement of porcine skin adhesion

observed for the conventional materials described above. For PET and PMMA plastics, attractive interactions caused by dipole-dipole interaction and hydrogen bonds between polyaspartamide and ester groups (hydrogen acceptors) on PET and PMMA may be responsible for the observed adhesive properties. As is well known, these plastic materials possess relatively hydrophobic surface character; thus, the polyaspartamide conjugated with hydrophobic octyl groups seemed to exhibit higher adhesive strength due to the enhanced hydrophobic interactions between the adhesive and adherends. In addition, π - π stacking interactions may represent another important interaction for the adhesion between DOPA-polyaspartamide and PS substrates. PS is a hydrocarbon-based polymer with aromatic benzene pendants.

Because it is similar to the human dermis, porcine skin is commonly used for adhesive testing of biomedical applications [28]. Figure 9 represents a typical adhesion test set-up, where two pieces of wet porcine skin are prepared (the left image of Figure 9). After spreading the polymer glue on the porcine skin

Figure 10. Lap shear strength test of polyaspartamide derivative glues on the porcine skin surface

Figure 11. Cell viability of polyaspartamide derivatives using MTT assay

surface, the samples were overlaid and compressed by a weight (90 g) for 10 min. As shown in Figure 10, the stress-strain behavior of PolyAspAm(DOPA/GABA) revealed a very low strength (4 kPa). This is probably due to the hydrophilic nature and water-swelling properties of the GABA functional groups, leading to a weak water boundary layer at the interfaces. The glue made from PolyAspAm(DOPA/OA) showed a much higher shear adhesive strength of 19 kPa, which is about 4.75 times greater than that of PolyAspAm(DOPA/GABA). Due to its moderately hydrophilic nature, the PolyAspAm(DOPA/EA) glue showed an adhesive value of 14 kPa, which falls in between the values of the two other glues.

The *vitro* cytotoxicity of three different polyaspartamide derivatives of PolyAspAm(DOPA/GABA), PolyAspAm(DOPA/EA) and PolyAspAm(DOPA/OA) were assessed using the MTT assay. The 293T cell line was used. It was suggested that the cell viability was determined to be nearly above 80% at all five different concentrations for these three polymers (Figure 11). This result indicated that the prepared polyaspartamide derivative polymers have low cytotoxicity and are well biocompatible with potential usefulness in biomedical applications.

4. Conclusions

In this study, biomimetic dopamine-conjugated polyaspartamides were synthesized and characterized as novel adhesive polymers. These wet polymer glues showed strong adhesion (0.1–0.4 MPa) on various daily-life materials (aluminum foil, glass, and paper) as well as on common plastic substrates. Compared to

the glues with relatively hydrophilic groups (GABA and EA), the polyaspartamide glue with a hydrophobic alkyl group (OA) exhibited higher adhesive strength values for most of the substrates. Furthermore, these polymer glues were applied to biological porcine skin and demonstrated adhesion strengths of 15–20 kPa with EA- and OA-conjugated derivatives. In conclusion, molecularly-engineered DOPA-polyaspartamides possess great potential to be used as versatile polymeric adhesives for both industrial and biomedical applications.

Acknowledgements

This work was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF), funded by the Ministry of Education, Science and Technology (NRF-2016R1D1A1A09918727).

References

- [1] Silverman H. G., Roberto F. F.: Understanding marine mussel adhesion. *Marine Biotechnology*, **9**, 661–681 (2007).
<https://doi.org/10.1007/s10126-007-9053-x>
- [2] Serrero A., Trombott S., Bayon Y., Gravagna P., Montanari S., David L.: Polysaccharide-based adhesive for biomedical applications: Correlation between rheological behavior and adhesion. *Biomacromolecules*, **12**, 1556–1566 (2011).
<https://doi.org/10.1021/bm101505r>
- [3] Heiss P. C., Kraus R., Schluckebier D., Stiller A.-C., Wenisch S., Schnettler R.: Bone adhesives in trauma and orthopedic surgery. *European Journal of Trauma*, **32**, 141–148 (2006).
<https://doi.org/10.1007/s00068-006-6040-2>
- [4] Mehdizadeh M., Yang J.: Design strategies and applications of tissue bioadhesives. *Macromolecular Bioscience*, **13**, 271–288 (2013).
<https://doi.org/10.1002/mabi.201200332>
- [5] Duarte A. P., Coelho J. F., Bordado J. C., Cidade M. T., Gil M. H.: Surgical adhesives: Systematic review of the main types and development forecast. *Progress in Polymer Science*, **37**, 1031–1050 (2012).
<https://doi.org/10.1016/j.progpolymsci.2011.12.003>
- [6] Waite J. H.: Nature's underwater adhesive specialist. *International Journal of Adhesion and Adhesives*, **7**, 9–14 (1987).
[https://doi.org/10.1016/0143-7496\(87\)90048-0](https://doi.org/10.1016/0143-7496(87)90048-0)
- [7] Leng C., Liu Y., Jenkins C., Meredith H., Wilker J. J., Chen Z.: Interfacial structure of a DOPA-inspired adhesive polymer studied by sum frequency generation vibrational spectroscopy. *Langmuir*, **29**, 6659–6664 (2013).
<https://doi.org/10.1021/la4008729>

- [8] Wei W., Yu J., Broomell C., Israelachvili J. N., Waite J. H.: Hydrophobic enhancement of dopa-mediated adhesion in a mussel foot protein. *Journal of the American Chemical Society*, **135**, 377–383 (2012).
<https://doi.org/10.1021/ja309590f>
- [9] Lu Q., Danner E., Waite J. H., Israelachvili J. N., Zeng H., Hwang D. S.: Adhesion of mussel foot proteins to different substrate surfaces. *Journal of the Royal Society Interface*, **10**, 20120759/1–20120759/12 (2013).
<https://doi.org/10.1098/rsif.2012.0759>
- [10] Kim B. J., Oh D. X., Kim S., Seo J. H., Hwang D. S., Masic A., Han K. D., Cha H. J.: Mussel-mimetic protein-based adhesive hydrogel. *Biomacromolecules*, **15**, 1579–1585 (2014).
<https://doi.org/10.1021/bm4017308>
- [11] Zhao H., Robertson N. B., Jewhurst S. A., Waite J. H.: Probing the adhesive footprints of *Mytilus californianus* byssus. *Journal of Biological Chemistry*, **281**, 11090–11096 (2006).
<https://doi.org/10.1074/jbc.M510792200>
- [12] Zhao H., Waite J. H.: Linking adhesive and structural proteins in the attachment plaque of *Mytilus californianus*. *Journal of Biological Chemistry*, **281**, 26150–26158 (2006).
<https://doi.org/10.1074/jbc.M604357200>
- [13] Li L., Smitthipong W., Zeng H.: Mussel-inspired hydrogels for biomedical and environmental applications. *Polymer Chemistry*, **6**, 353–358 (2014).
<https://doi.org/10.1039/C4PY01415D>
- [14] Heo J., Kang T., Jang S. G., Hwang D. S., Spruell J. M., Killops K. L., Waite H. J., Hawker C. J.: Improved performance of protected catecholic polysiloxanes for bioinspired wet adhesion to surface oxides. *Journal of the American Chemical Society*, **134**, 20139–20145 (2012).
<https://doi.org/10.1021/ja309044z>
- [15] Li L., Zeng H.: Marine mussel adhesion and bio-inspired wet adhesives. *Biotribology*, **5**, 44–51 (2016).
<https://doi.org/10.1016/j.biotri.2015.09.004>
- [16] Chen W., Leung V., Kroener H., Pelton R.: Polyvinylamine–phenylboronic acid adhesion to cellulose hydrogel. *Langmuir*, **25**, 6863–6868 (2009).
<https://doi.org/10.1021/la900131g>
- [17] Kaneko D., Wang S., Taira S., Hiraishi N., Tateyama S., Yasaki K., Miyasato A., Tsuge A., Kaneko T.: High-performance biocompatible adhesives from plant-derived materials. in ‘2013 International Symposium on Micro-NanoMechatronics and Human Science (MHS), Nagoya, Japan’ 1–3 (2013).
<https://doi.org/10.1109/mhs.2013.6710441>
- [18] Waite J. H., Tanzer M. L.: Polyphenolic substance of *Mytilus edulis*: Novel adhesive containing L-dopa and hydroxyproline. *Science*, **212**, 1038–1040 (1981).
<https://doi.org/10.1126/science.212.4498.1038>
- [19] Lee H., Dellatore S. M., Miller W. M., Messersmith P. B.: Mussel-inspired surface chemistry for multifunctional coatings. *Science*, **318**, 426–430 (2007).
<https://doi.org/10.1126/science.1147241>
- [20] Ye Q., Zhou F., Liu W.: Bioinspired catecholic chemistry for surface modification. *Chemical Society Reviews*, **40**, 4244–4258 (2011).
<https://doi.org/10.1039/c1cs15026j>
- [21] Guvendiren M., Brass D. A., Messersmith P. B., Shull K. R.: Adhesion of DOPA-functionalized model membranes to hard and soft surfaces. *The Journal of Adhesion*, **85**, 631–645 (2009).
<https://doi.org/10.1080/00218460902997000>
- [22] Stepuk A., Halter J. G., Schaetz A., Grass R. N., Stark W. J.: Mussel-inspired load bearing metal–polymer glues. *Chemical Communications*, **48**, 6238–6240 (2012).
<https://doi.org/10.1039/c2cc31996a>
- [23] Matos-Pérez C. R., White J. D., Wilker J. J.: Polymer composition and substrate influences on the adhesive bonding of a biomimetic, cross-linking polymer. *Journal of the American Chemical Society*, **134**, 9498–9505 (2012).
<https://doi.org/10.1021/ja303369p>
- [24] White J. D., Wilker J. J.: Underwater bonding with charged polymer mimics of marine mussel adhesive proteins. *Macromolecules*, **44**, 5085–5088 (2011).
<https://doi.org/10.1021/ma201044x>
- [25] Ninan L., Monahan J., Stroschne R. L., Wilker J. J., Shi R.: Adhesive strength of marine mussel extracts on porcine skin. *Biomaterials*, **24**, 4091–4099 (2003).
[https://doi.org/10.1016/S0142-9612\(03\)00257-6](https://doi.org/10.1016/S0142-9612(03)00257-6)
- [26] Ai Y., Wei Y., Nie J., Yang D.: Study on the synthesis and properties of mussel mimetic poly(ethylene glycol) bioadhesive. *Journal of Photochemistry and Photobiology B: Biology*, **120**, 183–190 (2013).
<https://doi.org/10.1016/j.jphotobiol.2012.10.012>
- [27] Sharma B., Fermanian S., Gibson M., Unterman S., Herzka D. A., Cascio B., Coburn J., Hui Y. A., Marcus N., Gold E. G., Elisseff J. H.: Human cartilage repair with a photoreactive adhesive-hydrogel composite. *Science Translational Medicine*, **5**, 167/1–167/6 (2013).
<https://doi.org/10.1126/scitranslmed.3004838>
- [28] Chung H., Grubbs R. H.: Rapidly cross-linkable DOPA containing terpolymer adhesives and PEG-based cross-linkers for biomedical applications. *Macromolecules*, **45**, 9666–9673 (2012).
<https://doi.org/10.1021/ma3017986>
- [29] Jo S. H., Sohn J. S.: Biomimetic adhesive materials containing cyanoacryl group for medical application. *Molecules*, **19**, 16779–16793 (2014).
<https://doi.org/10.3390/molecules191016779>
- [30] Giammona G., Carlisi B., Palazzo S.: Reaction of α , β -poly(*N*-hydroxyethyl)-DL-aspartamide with derivatives of carboxylic acids. *Journal of Polymer Science Part A: Polymer Chemistry*, **25**, 2813–2818 (1987).
<https://doi.org/10.1002/pola.1987.080251016>
- [31] Giammona G., Cavallaro G., Fontana G., Pitarresi G., Carlisi B.: Coupling of the antiviral agent zidovudine to polyaspartamide and in vitro drug release studies. *Journal of Controlled Release*, **54**, 321–331 (1998).
[https://doi.org/10.1016/S0168-3659\(98\)00020-0](https://doi.org/10.1016/S0168-3659(98)00020-0)

- [32] Craparo E. F., Teresi G., Licciardi M., Bondi M. L., Cavallaro G.: Novel composed galactosylated nanodevices containing a ribavirin prodrug as hepatic cell-targeted carriers for HCV treatment. *Journal of Biomedical Nanotechnology*, **9**, 1107–1122 (2013).
<https://doi.org/10.1166/jbn.2013.1608>
- [33] Pitarresi G., Palumbo F. S., Calabrese R., Craparo E. F., Giammona G.: Crosslinked hyaluronan with a protein-like polymer: Novel bioresorbable films for biomedical applications. *Journal of Biomedical Materials Research: Part A*, **84**, 413–424 (2008).
<https://doi.org/10.1002/jbm.a.31316>
- [34] Vlasák J., Rypáček F., Drobník J., Saudek V.: Properties and reactivity of polysuccinimide. *Journal of Polymer Science: Polymer Symposia*, **66**, 59–64 (2007).
<https://doi.org/10.1002/polc.5070660109>
- [35] Wang B., Jeon Y. S., Park H. S., Kim J. H.: Self-healable mussel-mimetic nanocomposite hydrogel based on catechol-containing polyaspartamide and graphene oxide. *Materials Science and Engineering: C*, **69**, 160–170 (2016).
<https://doi.org/10.1016/j.msec.2016.06.065>
- [36] Lu D., Zhang Y., Li T., Li Y., Wang H., Shen Z., Wei Q., Lei Z.: The synthesis and tissue adhesiveness of temperature-sensitive hyperbranched poly(amino acid)s with functional side groups. *Polymer Chemistry*, **7**, 1963–1970 (2016).
<https://doi.org/10.1039/C5PY01844G>