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단신

$NaIO_4$를 사용한 도파민-수식 폴리아스팔트아미드의 산화적 젤화

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Oxidative Gelation of Dopamine-modified Polyaspartamides by $NaIO_4$

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초록: 도파민 및 에틸렌디아민의 폴리숙신이미드(polysuccinimide)와의 연속적인 개환 아미놀리시스 반응을 통해 카테콜 및 1차 아민기를 곁가지에 함유한 접착성 폴리아스팔트아미드를 합성하고, 산화제로서 $NaIO_4$를 사용한 상기 고분자 수용액의 산화적 젤화 반응을 관찰하였다. FTIR, UV-vis과 oscillatory rheometry를 이용하여 산화성 가교반응을 통한 젤 형성을 규명하고, 제조된 젤의 수팽윤도, 열중량분석(TGA) 및 SEM 모폴로지를 조사하였다.

Abstract: Novel adhesive polyaspartamides containing catechol and primary amine pendent groups were synthesized through successive ring-opening aminolysis reactions of dopamine (DOP) and ethylenediamine (EDA) with polysuccinimide (PSI). The oxidative gelation of aqueous dopamine-modified polyaspartamide was observed by adding $NaIO_4$ as the oxidizing reagent. FTIR, UV-vis and oscillatory rheometry was used to elucidate the oxidative cross-linking toward gel formation. The prepared gel was characterized by the swelling degree, thermogravimetric analysis (TGA), and by scanning electronic microscopy (SEM).

Keywords: dopamine-modified, polyaspartamide, oxidative gelation, adhesive.

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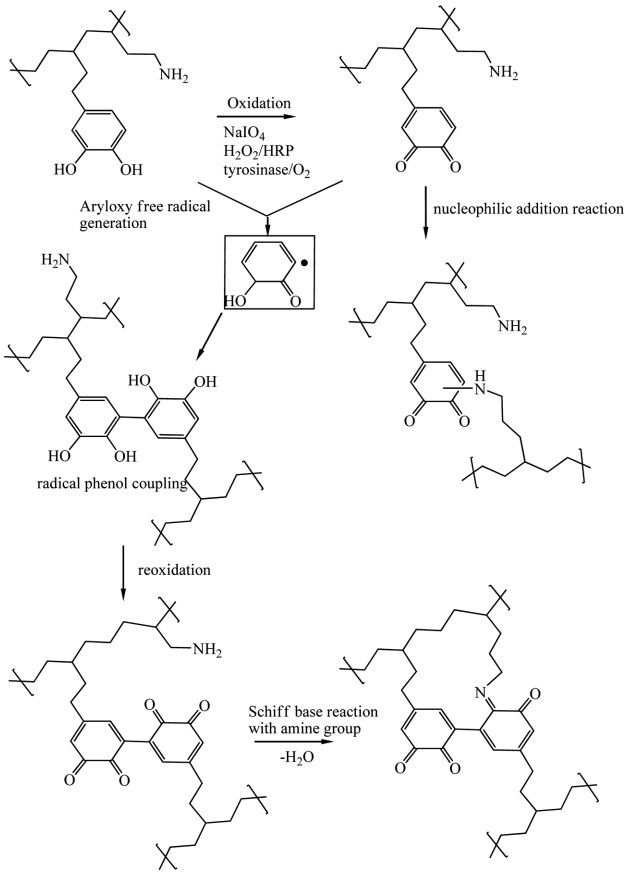
Introduction

In recent years, bio-inspired poly(dopamine) and dopamine-modified polymers have attracted considerable attention for their versatile utility in adhesive and surface modification of solid materials.[1] o-Dihydroxyphenyl (catechol) groups, the critical functional constituent of dopamine, have a very strong affinity to a variety of organic/inorganic surfaces (e.g. metal, metal oxide, ceramics, organic polymers) and even biomacromolecules.[2,3] Under oxidizing (or alkaline) conditions, the catechol group transforms its chemical structure to a quinone form which further participate in a variety of inter-molecular crosslinking reactions. It is known that the oxidized quinone can react with various functional groups including thiols, amines, and quinone itself *via* Michael-type additions, Schiff base reactions or aryl-aryl coupling[4,5] (Scheme 1). Currently, the adhesive method for versatile coatings inspired from the adhesive proteins found in mussels has been extensively studied by Messersmith group.[6,7] Also, dopamine or catechol functional groups have been incorporated into various polymers



Scheme 1. Crosslinking chemistry of dopamine-modified polymer.

intended for use as industrial, consumer, or medical adhesives by many authors.[8-14] This biomimetic anchor strategy seems quite robust for surface modification in many applications.

Polyaspartamides (PolyAspAm) include a wide range of amide derivatives of poly(aspartic acid), PAsp, which can be easily synthesized from polysuccinimide (PSI). The chemical modification of pendent groups can provide diverse polyaspartamide derivatives with specific properties.[15,16] These polymeric materials possess physicochemical characteristics suitable for the development of novel biomaterials in drug delivery system and tissue engineering in the forms of polymeric prodrugs, hydrogels or self-assembled nanoparticles.[17-20]

Previously, we reported a versatile coating of DOP-conjugated polyaspartamide onto various substrates in dilute aqueous solution.[21] In this study, the oxidative gelation behavior of concentrated polyaspartamide aqueous solution was investigated along with basic characterization of the gel.

Experimental

Materials. L-aspartic acid (98+%), *o*-phosphoric acid (98%), *N,N*-dimethylformamide (DMF, anhydrous 99.8%), dopamine hydrochloride (DOP), ethanolamine (EA, 99%), ethylenediamine (EDA, 99%), triethylamine (TEA, 99.5+%), sodium hydrosulfite (~85%), acetic acid (99+%), tris(hydroxymethyl)amino methane (Tris, 99.9+%), and sodium periodate ($NaIO_4$, 99.8+%), were purchased from Aldrich Chemical Co. Acetone was obtained from DaeJung Chemical Co. (Korea). All other chemicals purchased were of sufficient quality and used as received.

Synthesis of Polyaspartamide Derivative, PolyAspAm (DOP/EDA/EA). A typical synthetic procedure for dopamine-modified polyaspartamides from PSI, the precursor polymer, has already been published in our previous report (Scheme 2).[21] PSI was synthesized and purified using a previously reported procedure. The prepared PSI had a reduced viscosity of 0.45 dL/g in DMF. The estimated molecular weight was approximately 132000 Da, as calculated from an empirical equation relating the solution viscosity to the molecular weight. An approximate mole ratio of 19:24:57 for DOP:EDA:EA in the pendent group was determined from ^{1}H NMR measurements.

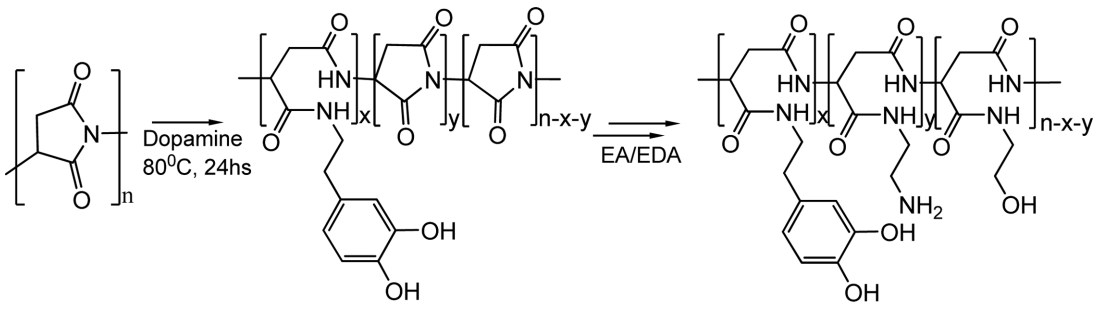
Characterization and Measurement. The ^{1}H NMR spectra were recorded on a Unity Inova-500 NMR spectrometer (Varian, Palo Alto, CA, USA) using D_2O as the solvent. FTIR spectra were obtained on a Spectrum 2000 FTIR spectrometer (Perkin Elmer, Norwalk, CT, USA). UV-vis spectra were obtained on a UV-visible spectrophotometer (Libra S22; Biochrom, Cambridge, UK).

Thermogravimetric analysis was carried out on a Perkin-Elmer DSC/TGA7 Series thermal analysis system at a heating rate of 10 °C/min under nitrogen. The modulus variation of the copolymer aqueous solutions was determined by dynamic mechanical analysis (Bohlin Rotational Rheometer). A polymer solution (125 mg/mL) in water was placed between a 20 mm diameter plate and a 100 mm diameter plate with a gap of 250 μm. Oscillation mode was employed with a stress of 0.4 Pa and a frequency of 1 rad/s.

The morphology of the freeze-dried polyAspAm(DOP/EDA/EA) gel was observed by field emission scanning electron microscopy (FE-SEM, JEOL 6320, Japan). Porous gel samples were mounted onto a metal stub with double-sided carbon tape and coated with Pt for 30 s under vacuum (10^{-3} Torr) using a plasma sputtering method (Ion sputter coater HC-21).

Results and Discussion

DOP or catechol functional group was incorporated into polyaspartamide to exploit the unique adhesive and crosslinking characteristics of the materials. In this study, the oxidative gelation behavior of concentrated aqueous solution of DOP-



Scheme 2. Synthesis of dopamine-modified polyaspartamide copolymer.

conjugated polyaspartamide was investigated along with the basic characterization of the gel.

Synthesis and Characterization of Dopamine-conjugated Polyaspartamides. As previously described, novel dopamine-containing polyaspartamide derivatives were synthesized from PSI through a successive aminolysis reaction with quantitative dopamine, EDA and excess EA. Figure 1 shows the ^{1}H NMR spectrum of a typical polyAspAm(DOP/EDA/EA). Peaks H were assigned to the aromatic protons of the dopamine phenyl group, and peaks f, g and d, e were assigned to the methylene proton of the EA and EDA pendants, respectively. The graft composition of each group in the polyaspartamide copolymer was determined from the integration ratios between H (δ = 6.3-6.8) and g (δ = 3.4-3.8) and e (δ = 2.9-3.1), and was found to correspond to a mole ratio of 19:24:57 for DOP:EDA:EA groups. FTIR spectral analysis of the prepared polyaspartamide derivative shows the characteristic strong amide I & II bands at 1649 and 1545 cm^{-1} along with N-H at 3305 cm^{-1}, which corresponds to the aspartamide backbone structure. The absorption bands of 1394 and 1293 cm^{-1} (phenolic C-O-H) indicate the characteristic functional groups of catechol (see Figure 4). Both ^{1}H NMR and FTIR analyses confirmed the structure of polyAspAm(DOP/EDA/EA).

As well documented in the literature, the oxidation of the catechol group is the key step, and is responsible for the polymerization and crosslinking chemistry of dopamine. To study the chemical change under oxidizing conditions, UV-vis spectroscopic measurement of the aqueous copolymer solution was performed. As shown in Figure 2, the absorption band of the catechol functional group appeared at λ_{max} = 290 nm in its unoxidized state. When the pH of the solution was increased to

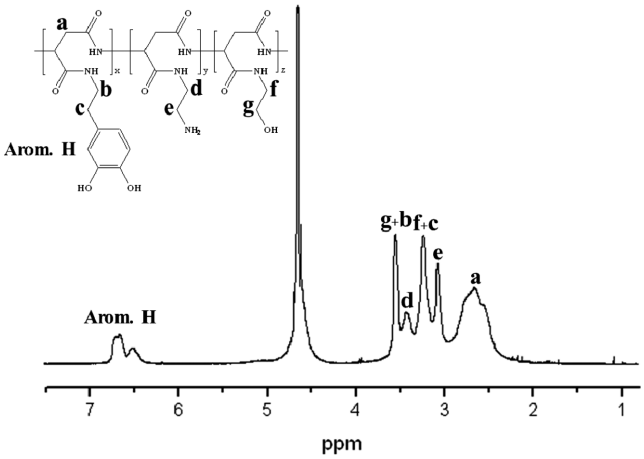


Figure 1. ^{1}H NMR spectrum of polyAspAm(DOP/EDA/EA).

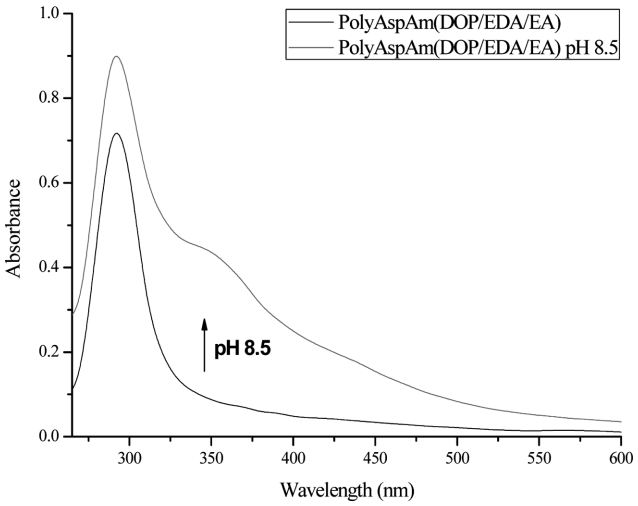


Figure 2. UV-vis spectra of aqueous copolymer solution.

pH 8.5, the absorption band at λ_{max} = 350 nm, which is responsible for the oxidized quinone form, was found to increase. Again, the dopamine chemistry involves the initial oxidation of catechol to semi-quinone or a quinone intermediate, which will induce the subsequent reactions such as phenolic radical coupling, Michael addition or Schiff-base reaction to provide the polymers an insoluble, crosslinked structure.

Gelation of Aqueous PolyAspAm(DOP/EDA/EA) Solution by $NaIO_4$. Figure 3 demonstrates the gelation of a dopamine-modified polyaspartamide solution by adding $NaIO_4$ as an oxidant. As the solution color turned dark brown, the polymer solution became a rubbery gel after a certain period time. Depending on the polymer concentration and the level of oxidant, the apparent gelation time changed. By using 200 mg/mL of polymer solution with 10 mg $NaIO_4$, gelation was observed in a minute as determined by a simple vial-tilting method. To investigate this gelation behavior more quantitatively, an oscillatory rheometer was used. With a solution concentration of 125 mg/mL, the content of oxidant $NaIO_4$ was varied in three different amounts of 2, 5, and 10 mg, respectively. From the

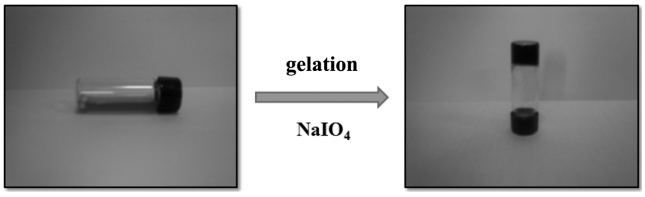


Figure 3. Oxidative gelation of dopamine-modified polyaspartamide solution.

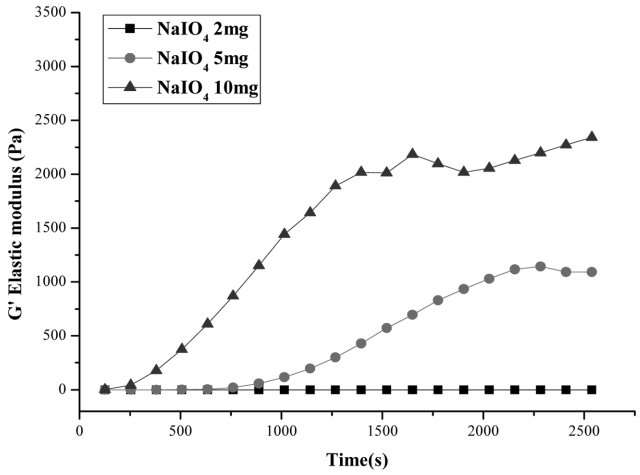


Figure 4. Modulus (or complex viscosity) change as a function of elapsed time.

rheometric measurement, the modulus (or complex viscosity) change was monitored as a function of elapsed time, and the results are plotted in Figure 4. When the oxidant level was relatively low (2 mg), bulk gelation was not observed even though the solution turned dark brown, probably due to an insufficient degree of crosslinking. When the oxidant amount was 5 mg, the modulus began to rise in about 700 s, and the value leveled off after 2000 s. When the oxidant amount was further increased to 10 mg, the modulus began to increase immediately upon mixing, and the increase leveled out in about 1300 s with a much higher modulus value. As can be expected, the gelation time is dependent on the level of oxidant and decreases with increasing oxidant quantity.

Characterization and Properties of DOP-Polyaspartamide Gel. The prepared gel was washed with PBS and distilled water several times and then freeze dried to give a hard and brittle sponge. Figure 5 shows the FTIR spectra of polymer (before oxidation) and the crosslinked gel (after oxidation). As described previously in the introduction part, the crosslinking reaction is initiated by the catechol oxidation to the quinone. The quinones, then, are supposed to undergo a complex inter-molecular reactions including aryl-aryl coupling and Michael addition or Schiff-base formation by adjacent amine groups to result in a crosslinked gel. The bands at 1394 and 1293 cm^{-1} corresponding to catechol C-O-H, and broad band at around 3300-3400 cm^{-1} of O-H and N-H were found to be decreased, suggesting the expected chemical change upon oxidative gelation. Figure 6 shows the swelling curves of the prepared gels in PBS (pH 7.4). The water absorbency or swelling ratio was observed to be 7-12 g/g. A SEM photograph of the dry gel is shown in Figure 7. An irregular porous morphology with a plate-like wall structure was observed. Figure 8 shows the TGA thermograms of the original polymer and its crosslinked gel produced using the oxidative process. The gel obtained by oxidant $NaIO_4$ showed an increased thermal stability as noticed from the shift of the thermal degradation curve to a higher temperature by approximately 30 ºC. The thermal degradation temperature of the original polymer with a T_{onset} of ~230 ºC has increased to 258.5 ºC. This improved thermal stability of gel materials must be due to the development of a network structure induced by the catechol oxidation and the following crosslinking reactions.

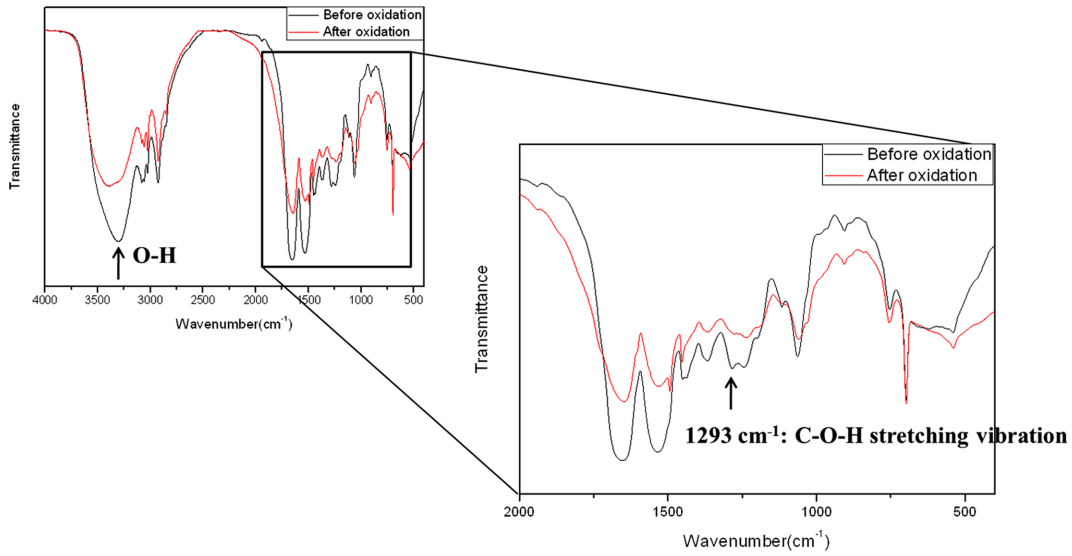


Figure 5. FTIR spectra of polyAspAm(DOP/EDA/EA) and its crosslinked gel.

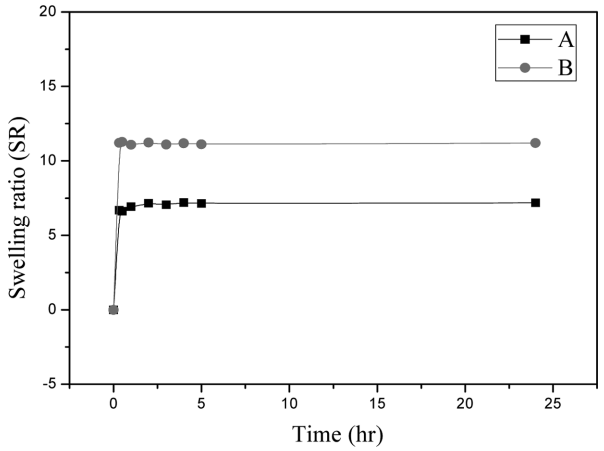


Figure 6. Swelling curves of the prepared gels in PBS (pH 7.4) (A: $NaIO_4$ 10 mg, B: $NaIO_4$ 5 mg).

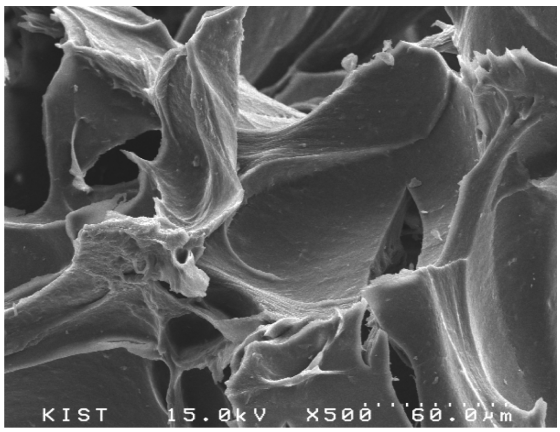


Figure 7. SEM morphology of dry gel scaffold (gelled by $NaIO_4$ 5 mg).

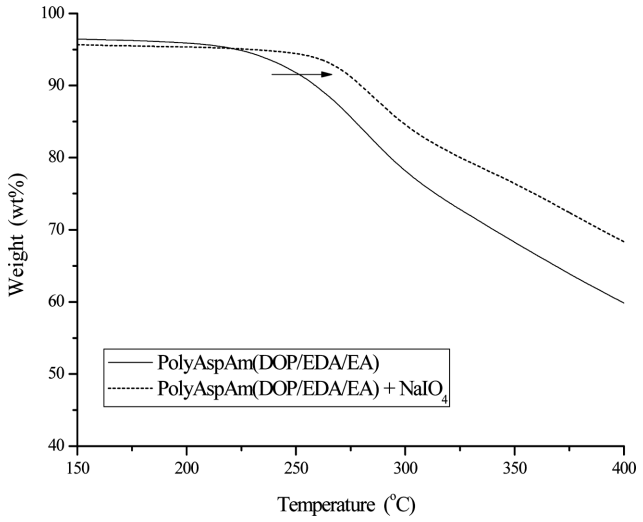


Figure 8. TGA thermograms of polyAspAm and its crosslinked gel.

Conclusions

Oxidative gelation behavior of novel adhesive copolymers based on polyaspartamide containing catechol and primary amine pendants was investigated. The gelation of aqueous polymer solutions was observed by the addition of oxidant $NaIO_4$ and the behavior was monitored by oscillatory rheological measurement. The prepared gels possessed high thermal stability and a porous network morphology.

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