

폴리아스팔트아미드와 폴리(비닐 피롤리돈)의 상용블렌드 및 Semi-IPN 젤 제조

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Miscible Blend and Semi-IPN Gel of Poly(hydroxyethyl aspartamide) with Poly(*N*-vinyl pyrrolidone)

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초록: 폴리아스팔트아미드 [α, β -poly(2-hydroxyethyl-DL-aspartamides), PHEAs]는 폴리아미노산의 일종으로서 잠재적인 의학 및 약학분야에 응용가능한 생분해성 생체적합성 재료로 널리 연구되어 왔다. 본 연구에서는 PHEA와 폴리(비닐 피롤리돈)(PNVP)의 블렌드 및 semi-IPN 젤에 관하여 다루었다. 블렌드 필름은 용액 캐스팅법으로 제조되었다. 제조된 블렌드는 전 조성에서 투명하였으며 DSC를 통해 조성에 따라 단조롭게 변화하는 단일한 유리전이 온도가 관찰됨으로써 두 개 고분자가 서로 상용성이 있음을 확인하였다. 고분자간의 가능한 수소결합 상호작용을 FTIR을 이용하여 설명하였다. 한편, 일정 조성의 PHEA/PNVP 블렌드 용액을 헥사메틸렌디이소시아네이트(HMDI)를 가교제로 사용하여 semi-IPN 타입의 하이브리드 젤을 제조하고, 제조된 젤의 팽윤 물성과 모폴로지를 조사하였다.

Abstract: PHEAs [α, β -poly(2-hydroxyethyl-DL-aspartamides)], a class of poly(amino acid), have been widely studied as biodegradable and biocompatible polymers for potential biomedical and pharmaceutical applications. In this study, we investigated a homogeneous blend of PHEA with poly(*N*-vinyl pyrrolidone) (PNVP) and its semi-IPN (semi-interpenetrating polymer network) gels. Blend films were prepared by a solution casting method. The resulting blends were totally transparent over the whole composition ranges and the single T_g , changing monotonously with composition, was observed by DSC to confirm the miscibility between these two polymers. FTIR was used to discuss the possible hydrogen-bonding interaction between polymers. In addition, semi-IPN type gels were prepared by chemical crosslinking of PHEA/PNVP blend solution using hexamethylene diisocyanate (HMDI) as a crosslinking reagent. The prepared gel was characterized by their swelling property and morphology.

Keywords: polyaspartamide, miscible blend, hydrogen-bonding, semi-IPN gel, PNVP, swelling behavior.

Introduction

Several different ways, including blend or composite with other materials, can be applied to improve or modify a given polymer properties. Blend of two polymers will have modified physical and mechanical properties different from those made of the individual polymers, depending on the degree of mixing.^{1,2} In many blend systems, a homogeneous phase is obtained due to the existence of specific interactions between the different polymeric components, which allows mixing on a molecular scale.³ One such interaction is hydrogen bonding,

which has been reported for many polymeric blends.⁴

Hydrogels are hydrophilic polymer networks which can absorb a large amount of water but are insoluble due to the fact that their molecules are crosslinked forming a network. Hydrogels have many desirable properties for applications in many different fields, such as biomedicine, agriculture, electrophoresis, water treatment, etc. Recently, there has been increasing interest in the use of hydrogels for novel drug and cell delivery and also as tissue engineering scaffold.⁵⁻¹⁰ Poly(*N*-vinyl pyrrolidone) (PNVP), a well-known hydrophilic polymer, has many biomedical applications such as a blood plasma extender, a carrier of drug delivery, a modifier for enzymes, and a copolymer in UV-curable bioadhesives due to its many outstanding properties and biocompatibility.¹¹ In addition, it

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has a favorable chelating property and is used in the drug and food field as a chelating agent. However, high water-solubility prevents PNVP from being shaped *in vivo*, so that PNVP was used mainly in the form of a crosslinked network. PNVP and its copolymer gels have been successfully used as a basic material for the manufacturing of contact lens and hydrogel wound dressing. On the other hand, the hydrogel, when it is crosslinked, becomes nonbiodegradable, which limits its use in the field of biomedical applications such as scaffold material for tissue engineering.

PHEA [α,β -poly(2-hydroxyethyl-DL-aspartamide)] and the derivative polymers have been widely studied for biomedical and pharmaceutical applications as drug delivery carrier, polymeric prodrug, and also the form of various hydrogels.¹²⁻²³ Poly(2-hydroxyethyl aspartamide) (PHEA) is a class of poly(amino acid) with hydroxyl pendent groups, which can be derived by coupling polysuccinimide with ethanolamine. PHEA has been proposed as a potential plasma extender and carrier for macromolecular prodrugs owing to its unique properties, such as biodegradability, water solubility, multipoint drug attachment, nontoxicity, nonantigenicity and biocompatibility. PHEA is freely soluble in water and various chemical derivatization or conjugation reaction is possible by using hydroxyl groups on the polymer backbone.

In our previous studies, the preparation of crosslinked gels from PHEA and various PHEA derivatives and their gel swelling property and stimuli responsive behavior have been investigated.^{18,19,24} PHEA and other derivative polymers could be crosslinked chemically by reacting hydroxyl groups of PHEAs with crosslinker molecules such as diisocyanate compound. Our group also reported on the preparation of PHEA/silica hybrid gels by using a sol-gel process, which provided a useful way to obtain organic/inorganic hybrid in crosslinked network form.²⁵ The resulting hybrids showed improved thermal and dimensional stability compared to neat PHEA.

In this work, we attempted blend of PHEA with PNVP among several different water-soluble and biocompatible polymers in order to modify and improve the properties of neat PHEA. In addition, semi-IPN hybrid gel was prepared by chemical crosslinking of PHEA/PNVP homogeneous blend to identify a new hybrid gel system with the swelling property and morphology.

Experimental

Materials. L-Aspartic acid (98+%) and *o*-phosphoric acid

(98%) were purchased from the Aldrich Chemical Co. PNVP ($M_w = 50000/M_w = 360000$) was purchased from Sigma-Aldrich Co. Ethanolamine (EA) (99+%), hexamethylene diisocyanate (HMDI, 98%), dibutyltin dilaurate (95%), *N,N'*-dimethylformamide (DMF) (anhydrous, 99.8%) were purchased from Sigma-Aldrich Co. The water was purified using a reverse osmosis system (Sartorius, arium 61315). All chemicals were of reagent grade and used without further purification.

Measurements. The FTIR spectra were obtained on a PerkinElmer FTIR spectrometer (Model SPECTRUM 2000). The thermal analyses were carried out on a PerkinElmer DSC/TGA7 Series thermal analysis system at the heating rate of 10 °C/min in nitrogen. The morphology of the prepared blend film was observed by scanning electron microscopy (ESEM Model XL30 ESEM-FEG, Phillips). The 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).

Synthesis of Polysuccinimide (PSI). High molecular weight polysuccinimide (PSI) was prepared by thermal condensation of L-aspartic acid (20 g) in the presence of *o*-phosphoric acid (20 g) under reduced pressure at 200 °C for 5 h. The reaction mixture was then cooled and DMF was added to dissolve the product. The resulting solution was precipitated in excess methanol and washed with distilled water to remove the residual phosphoric acid. The molecular weight of PSI was estimated to be approximately 120000 Da, as calculated from an empirical equation that relates the solution viscosity to the molecular weight.

Synthesis of α,β -Poly(2-hydroxyethyl-DL-aspartamide) (PHEA). 2 g of PSI was dissolved in 40 mL of DMF in a 50 mL three-necked round bottom flask with a nitrogen gas inlet and outlet. Excess ethanolamine (EA) was slowly added into the above-mentioned PSI solution with vigorous stirring. The solution was stirred at 25 °C for 2 h. Then 1.6 mL acetic acid was added. After 1 h, 50 mL of deionized water was added and stirred for other 0.5 h. Final solution was frozen and lyophilized.

Preparation of Blend Films. PHEA and PNVP were dissolved in anhydrous DMF at the concentration of 0.1 g/mL. PHEA and PNVP solution was mixed together by violent stirring for 8 h. The mass ratio between PHEA and PNVP was in the range from 1:9 to 9:1, respectively. Blend solutions then were casted on glass substrate, which were dried in an air-circled oven at 60 °C for 1 day to remove most of the solvent, and then had them totally dried in a vacuum oven at 80 °C for 2 days.

Preparation of Semi-IPN Hydrogels. Semi-IPN type crosslinked gel was prepared from PHEA-PNVP blend. Typically, 0.1 g of PHEA and 0.1 g of PNVP ($M_w=360000$) were dissolved in 2 mL DMF, and stirred to get a homogeneous solutions. The solutions were degassed by repeating vacuum and N_2 purge for several times. HMDI (each 20, 30, 40, 50 mol% of PHEA units) was added to the mixture and 20 μ L of dibutyltin dilaurate as the catalyst was added to the solution and stirred quickly for 1 min. The solutions were kept reacting for 2 h at 60 °C. Resulting gels were placed in a closed steel mesh and washed with a large amount of water. The gel samples were then freeze-dried to obtain white gel sponges.

Results and Discussion

We investigated the blend of PHEA with PNVP ($M_w=360000$), one of industrially important, water-soluble polymers. PNVP is a tertiary amide polymer which can function as strong hydrogen-bonding acceptor with nonbonding electron pairs. Blends were prepared by solution casting method. The resulting blend films were flexible and totally transparent over the whole composition ranges.

Figure 1 showed the DSC curves of the blend films with different mass ratio. The T_g values deduced from these curves are shown in Table 1. For neat PHEA and PNVP, the T_g s were 77

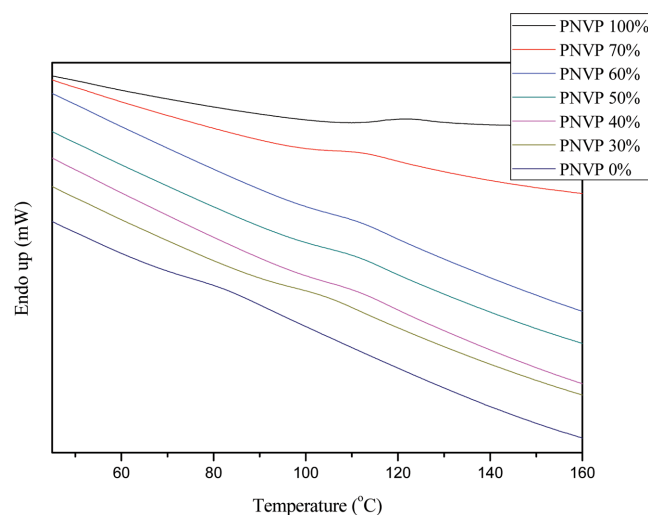


Figure 1. DSC thermograms of PHEA-PNVP blends.

Table 1. T_g Values of PHEA-PNVP Blends in Various Different Compositions

PHEA:PNVP	0:10	3:7	4:6	5:5	6:4	7:3	10:0
T_g (°C)	116	107	106	105	104	99	77

and 116 °C, respectively. For the all different blend compositions, single glass transition was observed in between those of two polymers, suggesting that PHEA and PNVP form a miscible blend system in whole composition range.

Figure 2 showed the TGA thermograms of PHEA-PNVP blend samples. PNVP is quite thermally-stable polymer, retaining weight up to about 400 °C. There showed some increment in the decomposition temperature of blend as the PNVP content increased in the blend composition. For this blend system, intermolecular interactions such as hydrogen-bond along with some other interactions, for example, chain entanglement, van der Waals force, can be applied between the two polymers, which might lead to the increase in their thermal stability.

Infrared spectrum can be used to reveal specific intermolecular interaction such as hydrogen-bonding from spectral changes upon blending. Figure 3 shows the FTIR spectra of

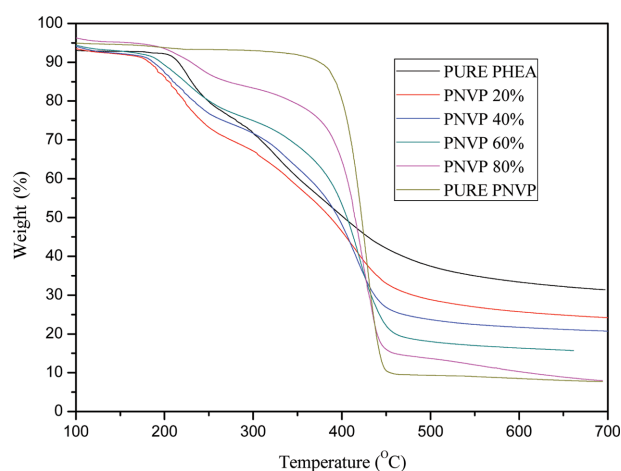


Figure 2. TGA thermograms of PHEA-PNVP blends.

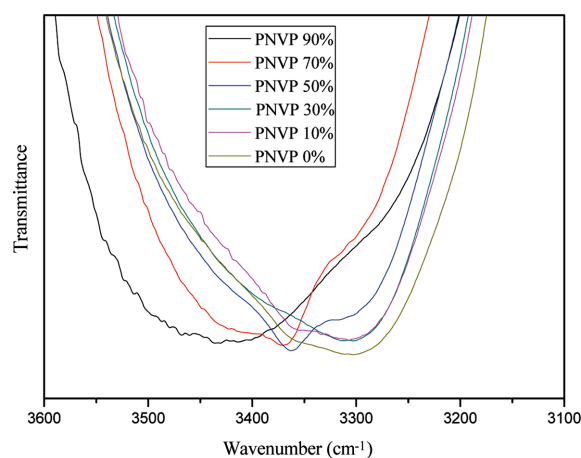


Figure 3. FTIR spectra of PHEA-PNVP blend systems.

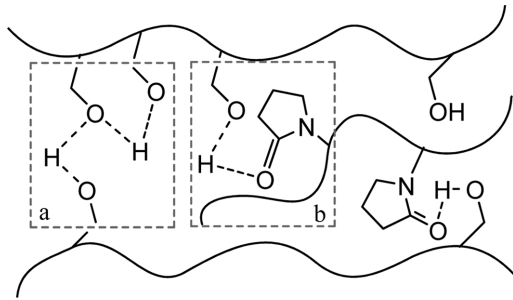


Figure 4. Schematic diagram of hydrogen-bonding in PHEA-PNVP blend.

PHEA-PNVP blend system in the range of 3250 and 3450 cm^{-1} , corresponding to the $-\text{OH}$ stretching absorption. The absorption band, originally centered at around 3300 cm^{-1} , decreased and seemed to shift toward higher wavenumber with the increment of PNVP content. This spectral change can be explained from the shift in the intra to intermolecular hydrogen-bonding interaction between two polymers; i.e. as PNVP, hydrogen-bond acceptor, was added, the hydrogen-bonding between pure PHEA are partially broken and replaced by ones between PHEA and PNVP. The schematic diagram of PHEA/PNVP hydrogen-bonding is shown in Figure 4. New interactions will reduce the density of hydrogen-bonded hydroxyl groups of PHEA by themselves, leaving some portion of free hydroxyl groups. Overall the hydrogen bonding interactions between two different polymers are considered to play a major role to achieve miscibility.

Preparation and Swelling Property of PHEA-PNVP Semi-IPN Gels. As we have discussed in previous section on the blend of PHEA with PNVP, these two polymers showed a homogeneous mixing in the whole composition range. Here, we prepared semi-IPN gel as the reaction shown in Scheme 1. Several different amount of HMDI, as a reactive crosslinker, was introduced to the solution of two component polymers to provide gels. The reaction between hydroxyl pendent groups on the PHEA with isocyanate group of HMDI to form urethane linkage is responsible for the formation of PHEA network within the PNVP matrix. The resulting gel network must

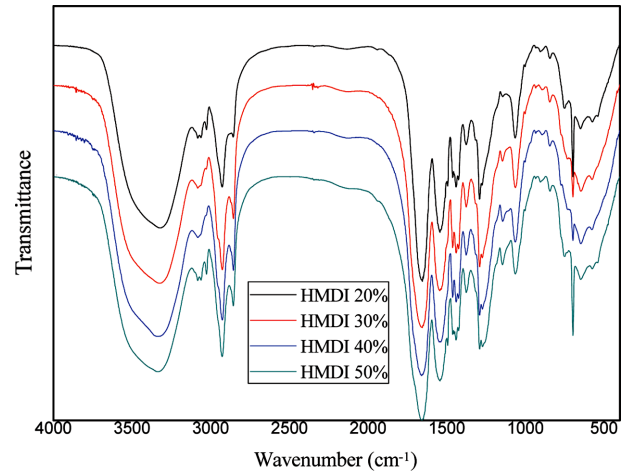
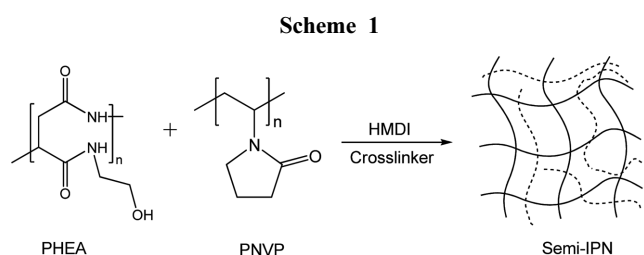


Figure 5. FTIR spectra of PHEA-PNVP semi-IPN gels.

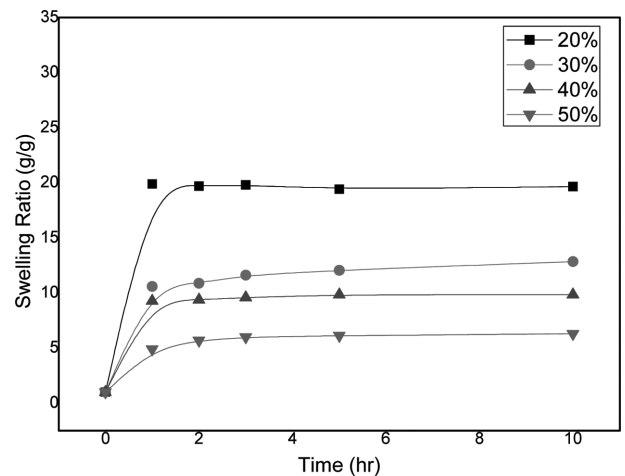


Figure 6. Swelling ratios of PHEA-PNVP semi-IPN gels with different HMDI contents.

have semi-IPN type as represented in Scheme 1. All the gel samples were obtained as transparent solid blocks in the vial. Figure 5 shows FTIR spectra of the PHEA-PNVP blend gels prepared with several different HMDI content. The characteristic absorption band of amide groups of PHEA backbone and the amide of pyrrolidone occurs at 1750 and 1652 cm^{-1} . The characteristic urethane bands appeared at 1350 cm^{-1} with increasing intensity upon HMDI content.

Swelling curves showed that the gel samples absorbed water very quickly and reach the equilibrium swelling in an hour (Figure 6). The swelling ratio was observed in the range of ca. 5-20 g/g. The swelling degree decreased gradually as the HMDI content increased from 20 to 50%, which are expected from the increasing crosslinking density of the gel network. The swelled hybrid gels possessed relatively good gel strength

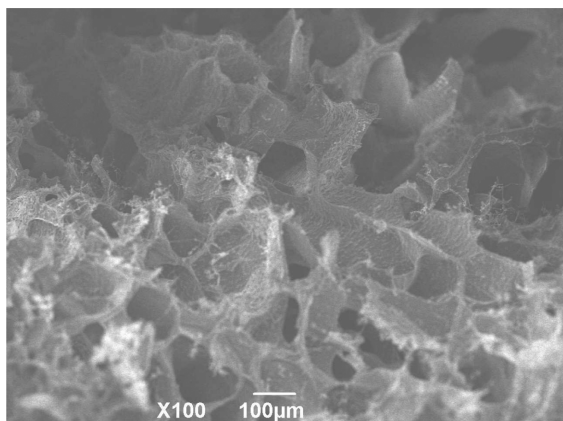


Figure 7. Morphology of freeze-dried PHEA-PNVP hybrid gel.

compared to neat PHEA gel previously made, which might be due to the very high molecular weight PNVP chains comingled with crosslinked PHEA in their semi-IPN structure. Characteristic gel morphology of the freeze-dried samples of water-swollen hydrogel was observed by scanning electron microscopy as shown in Figure 7. Microporous structure of blend gel with tens of micron size pores can be compared with basically nonporous neat PNVP hydrogel.

Conclusions

Blend films based on PHEA and commercially available PNVP were prepared. Both the thermal properties and hydrogen-bonding interaction were studied by TGA, DSC and FTIR. PHEA blending with PNVP, of all composition range, provided transparent films, and all showed well miscible systems which were well supported by the single T_g value of each composition. The existence of hydrogen bonding in the PHEA/PNVP blend system was proved by the FTIR analysis. Semi-IPN gel was prepared by chemical crosslinking of PHEA/PNVP blend solution using HMDI as the crosslinking reagent. The prepared gel showed swelling degrees in the range 5~20 g/g water, depending on the crosslinker content. The swelled gel possessed relatively good gel strength and well-connected microporous morphology.

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