Preparation and Characterization of Interpenetration Polymer Network Films Based on Poly(vinyl alcohol) and Poly(acrylic acid) for Drug Delivery

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ABSTRACT: A series of full interpenetrating polymer network (full-IPN) films of poly(acrylic acid) (PAA)/poly (vinyl alcohol) (PVA) were prepared by radical solution polymerization and sequential IPN technology. Attenuated total reflectance-Fourier transform infrared spectroscopy, swelling properties, mechanical properties, morphology, and glass transition temperature of the films were investigated. FTIR spectra analysis showed that new interaction hydrogen bonds between PVA and PAA were formed. Swelling property of the films in distilled water and different pH buffer solution was studied. Swelling ratio increased with increasing PAA content of IPN films in all media, and swelling ratio decreased with increasing PVA crosslink degree. Tensile strength and elongation at break related not only to the constitution of IPNs but also to the swelling ratio of IPNs. Mechanical property of glutaraldehyde (0.5%) for poly(vinyl alcohol) crosslinking was better than that of glutaraldehyde (1.0%). DSC of the IPN films showed only a single glass transition temperature (T_g) for each sample, and T_g data showed a linear relationship with network composition. Morphology was observed a homogeneous structure, indicating the good compatibility and miscibility between PAA and PVA. Potential application of the IPN films in controlled drug delivery was also examined using crystal violet as a model drug. The release rate of the drug was higher at 37°C than 25°C for all IPNs and also increased slightly with decreasing of poly(acrylic acid) content. © 2008 Wiley Periodicals, Inc. J Appl Polym Sci 108: 3836–3842, 2008

Key words: interpenetrating polymer network; poly(vinyl alcohol); poly(acrylic acid); films; drug release

INTRODUCTION

An interpenetrating polymer network (IPN) is defined as the combination of two polymers that has the following two characteristics: (1) one of the polymers must be synthesized or cross-linked in the immediate presence of the other polymer, and (2) the combination must provide the possibility of effectively producing advanced multicomponent polymeric systems with new property profiles.[1] Moreover, IPNs for hydrogels have also been largely studied.[2–4] Hydrogels are crosslinked three-dimensional hydrophilic polymer networks that swell but do not dissolve when they mix with water. The water uptake by hydrogels is sensitive to external environment, including the temperature, the pH, the ionic strength, and the electric field. Therefore, they are extensively applied in biomedical field. Especially, in drug-delivery systems, they received much attention because they could maximize the healing effect to maintain the effective drug concentration in the blood for a prolonged period of time. To date, many types of hydrogels as drug carriers have been widely investigated.[5–14] Among the hydrogels, however, considerable research attention has been focused on so-called smart hydrogels, which can transfer their volume in response to environmental stimuli and thus can modify drug release.

PAA is a pH sensitive and electrically sensitive material and also widely applied as biomedical material,[15–17] because it has carboxylic acid groups that could develop different intermolecular interaction such as hydrogen bonds, ion–ion, and dipole–ion with other polymers or molecules.

PVA is a water-soluble poly hydroxyl polymer, widely used in practical applications in biomedicine and biochemistry due to easy preparation, excellent chemical resistance, biocompatibility, and complete biodegradability.[18–22] In our system, PVA was chosen because of its strength, good film-forming property, and long-term temperature and pH stability.

Lee and coworkers have reported that PVA/PAA IPNs prepared by using ultraviolet (UV) irradiation and the freezing–thawing method[15,23–26] for physical crosslinking of PVA and study the swelling kinetics,[23] drug release,[15] and various solute penetration.[24]

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Besides, there have been several investigations on hydrogel or membrane of IPN composed of PVA/PAA prepared by azo radical initiating system[27–30] and chemical crosslinking for PVA. These types of hydrogels are mainly used in solute permeation[27–29] and pervasive separation.[30] In this article, we used radical solution polymerization and sequential IPN technology of redox-initiating system and chemical crosslinking for PVA to prepare a series of full IPN films of PAA/PVA and studied the characteristics and potential application for drug delivery.

EXPERIMENTAL

Materials

Acrylic acid (AA), analyst reagent (Beijing Chemical Plant, China), was distilled under reduced pressure before use. PVA (98–99% hydrolyzed, molecular weight 88,000–97,000 g/mol) and *N*,*N*′-methylenebisacrylamide (MBA, 99%+) were purchased from Alfa Aesar. *N*,*N*,*N*,*N*′-tetramethylethylen-diamine (TEMED, 99%) was obtained from Aldrich Chemicals. Glutaraldehyde (GA, 25% aq. Soln) was provided by Avocado Research Chemicals. Ammonium persulfate (APS) and hydrochloric acid were obtained from Beijing Chemical Plant. Crystal violet (CV) was supplied by Fluka. Except for AA, all other regents were of analytical grade and were used as received.

Preparation of PAA/PVA IPN films

PAA/PVA IPN hydrogel films were prepared by radical solution polymerization and sequential IPN technology. The PAA network was first synthesized in PVA aqueous solution by redox-initiating system. Then, PVA network as a secondary network was formed by chemical crosslinking. PVA was dissolved in deionized water and maintained at 90°C for 2 h to obtain 8 wt % PVA aqueous solution. AA monomer, 1.0 wt % MBA, as a crosslinking agent for the crosslinking of AA, and 1.0 wt % TEMED, as an accelerator, were mixed with PVA aqueous solution with mechanical stirring. The mass ratios of PVA to PAA were adjusted to 30 : 70, 40 : 60, 50 : 50, 60 : 40, and 70 : 30, respectively. The total polymer concentration was 5 wt % in the mixed reactive solution. The mixed solution was initiated by adding 1.0 wt % APS as an initiator after 30 min under nitrogen atmosphere and then reacted at 50°C for 24 h. After polymerization, the certain weight of reactant solution under stirring was added 0.5 or 1.0 wt % GA and the same weight of 1*N* HCl solution with GA. At room temperature, PVA was crosslinked in the presence of PAA, using GA and HCl as a crosslinking agent and catalyzer at room temperature, respectively. After 1 h, the solution was transferred onto a known area petri dishes and dried for 8 h at 50°C in an oven. The film obtained was immersed in water for 2 days to eliminate any possible residual HCl and GA and then dried at room temperature, and at last dried under vacuum at 30°C for 3 days.

Swelling studies

The dried film samples were immersed in distilled water or buffer solution of different individual pH at room temperature to swell to reach the equilibrium sorption. Weight after slightly removed the surface water of the film by using filter paper. The swelling ratio was calculated by the following equation:

$$\text{Swelling ratio} = (W_s - W_d)/W_d$$

where W_d is the weight of dried sample and W_s is the weight of swollen samples.

ATR-FTIR studies

Attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR) of the dried film samples was measured with Bruker Vertex 70 FTIR spectrophotometer, and the spectra were signal averaged over 128 scans at a resolution of 4 cm^{-1}, inspect was DTGS.

Mechanical properties

The tensile measurement was conducted on INSTRON 1121 USA material test machine with a tensile rate of 20 mm/min at room temperature. After the films were fully swelled, the sample strips were 40 mm length, about 10 mm width, with 20 mm distance between the two clamps. Three or four measurements were carried out for every sample, and the mean value was obtained.

Morphology studies

Scanning electron micrograph of the dried films was taken with a scanning electron micrograph (XL30 ESEM FEG) to study the morphology of films. The cross sections were observed and photographed after cracked in liquid N_2 and then sputter coated with gold.

Thermal characterization

DSC (differential scanning calorimetry) was measured on PE 7 Series Thermal Analysis System (USA). About 10 mg of dry film samples were scanned from 20 to 210°C at a heating rate of 10°C/min under N_2 flow. The first scan was used to remove the hot history and remains matter, the T_g was obtained from the second scan, and the value was taken from the midpoint of change in the specific heat.

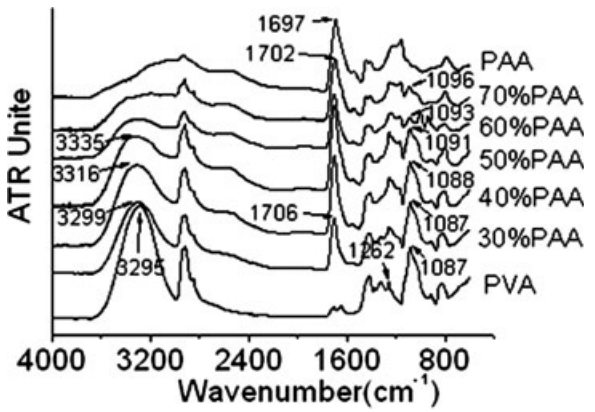

Figure 1 ATR-FTIR spectra of PAA/PVA IPNs. The spectra of PVA and PAA are included for comparison.

Drug-release studies

CV was used as a model drug. About 40 mg of dry films were equilibrated in drug solution of 30 mg /10 mL at room temperature for 2 days to load the drug into the IPN films. Then the loaded-drug gels were removed from the drug solution and dried under vacuum at 30°C for 3 days. The drug-release experiment was carried out by transferring the dried drug-loaded films in 10 mL 9% NaCl at 25 or 37°C. The IPN films loaded with CV were placed in the release medium and repeatedly removed from the solution and then transferred into 10 mL fresh release medium at each fixed time interval. The released drug was analyzed by UV spectrophotometer Perkin Elmer Lambda 900, USA, at 598 nm. The release amount was calculated by previously established calibration curve.

RESULTS AND DISCUSSION

ATR-FTIR of PAA/PVA IPN films

In this study, PAA/PVA IPN hydrogel films were prepared by radical solution polymerization and sequential IPN technology. The PAA network was first synthesized in aqueous solution of PVA. Then PVA network as a secondary network was formed by chemical crosslinking using GA as a crosslinking agent.

As can be seen from the ATR-IR spectra of the samples (Fig. 1), several differences were apparent with different composition of IPNs. The peak of O—H stretching vibration at 3295 cm^{-1} from pure PVA films, when compared with that of IPNs, was gradually shifted to higher wave number, weakened, and broadened with increasing PAA content in IPNs. The wave number of the peak from 3295 cm^{-1} for pure PVA shifted to 3299, 3316, and 3335 cm^{-1} at 30% PAA, 40% PAA, and 50% PAA, respectively. At 60% PAA, the peak had become a broad peak. This peak, at last, was so broad and weak as to almost overlap with the broad peak of 3500–2400 cm^{-1} of COOH with an increase of PAA content, and then it was not evident in 70% PAA in IPNs. This indicated that hydrogen bonds interactions of PVA gradually replaced by hydrogen bonds interactions between PVA and PAA.

The C—O stretching vibration at 1262 cm^{-1} from pure PVA gradually became stronger and broader with the increasing of PAA content of IPNs because of the new intermolecular interaction hydrogen bonds of IPNs. The dissymmetry stretching vibration of C—O at 1087 cm^{-1} from pure PVA gradually shifted to higher wave number with an increase of PAA content. As we see, the wave number of the peak from 1087 cm^{-1} for pure PVA shifted to 1087, 1088, 1091, 1093, and 1096 cm^{-1} at 30% PAA, 40% PAA, 50% PAA, 60% PAA, and 70% PAA, respectively. Besides, the peak intensity apparently became weak in the structure of IPNs, especially in 60% PAA and 70% PAA. These showed the result of new hydrogen bonds of IPNs.

The dissymmetry stretching vibration of C=O of COOH from pure PAA, at 1697 cm^{-1}, had became 1702 cm^{-1} 70% PAA and shifted to high wave number in the structure of IPNs with increasing PVA content. At 30% PAA, it shifted the highest wave number 1706 cm^{-1}. This showed new strong hydrogen bonds interactions between PVA and PAA replaced hydrogen bonds interactions in the PAA. These differences indicated that new hydrogen bonds of IPNs were formed.

Swelling properties of PAA/PVA IPN film

The dried film samples were immersed in distilled water or different pH buffer solution at room temperature to swell to reach the equilibrium sorption. Weight after slightly removed the surface water of the film by using filter paper.

As can be seen from Figure 2, swelling ratio in water increased with increasing PAA content of

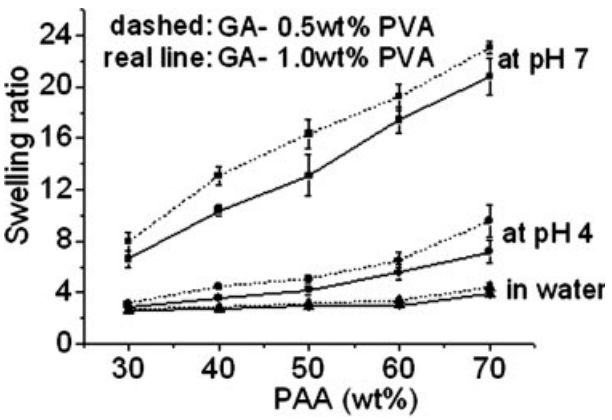

Figure 2 Swelling ratio of PAA/PVA IPN with different compositions in water and different pH solution. For all membranes, initiator and crosslinker are both 1.0 wt % PAA.

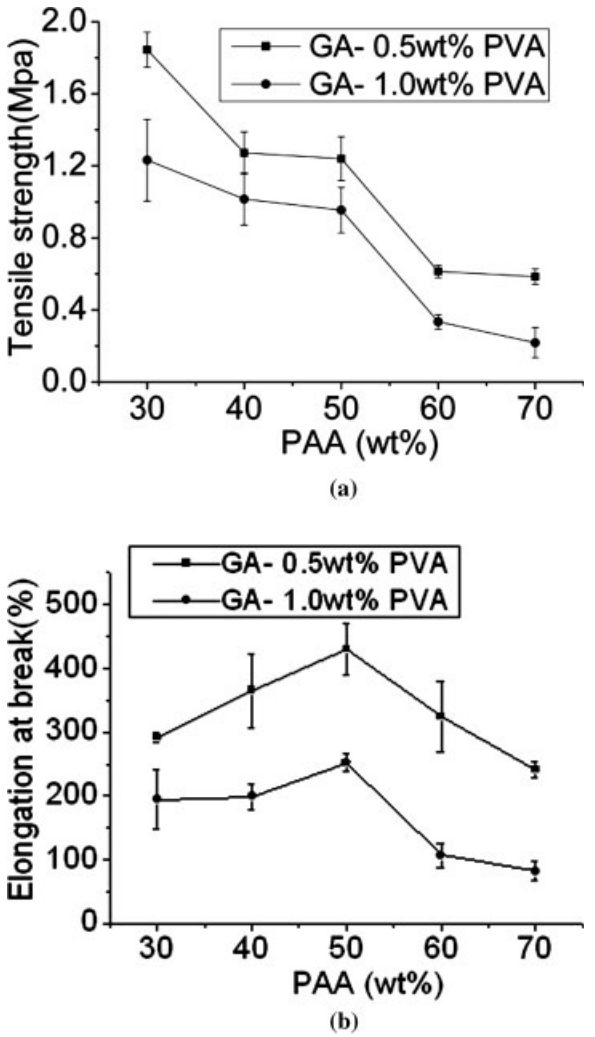

Figure 3 Mechanical properties of PAA/PVA IPN with different compositions. For all membranes, initiator and crosslinker are both 1.0 wt % PAA.

PAA/PVA IPN films, it was caused that adding PAA switched to more hydrophilic.

Because of the presence of carboxylic acid, the swelling behavior of the PAA hydrogel was highly dependent on the pH of the surrounding medium. Because the pK_a of PAA was 4.75, so at pH 4 acetate buffer solution, the carboxyl groups of PAA, which exist as a hydrated state, formed strong hydrogen bonds with water and so partially destroyed the interaction hydrogen bonds of IPNs, the swelling ratio increased at pH 4 than in water. At pH 7 phosphate buffer solution, because of the ionic repulsion of carboxylic ions and thus dissociation of hydrogen bonding of IPNs, therefore it induced the significant increase of the water uptake. So, the highest swelling ratio of IPN film was achieved at pH 7 phosphate buffer solution in various medium.

At the same time, the more PAA content in the IPNs, the higher the swelling ratio in various medium. Meanwhile, we can also see that swelling ratio decreased with increasing PVA crosslink degree (GA from 0.5 wt % to 1.0 wt %). This was because that crosslink decreased the number of hydrophilic OH and increased the number of nodes of networks.

Mechanical properties of PAA/PVA IPN film

Figure 3 showed the tensile strength and elongation at break as a function of the PAA content. We can see that the tensile strength decrease and elongation at break have a maximum with increasing PAA content. This indicated that tensile strength and elongation at break related not only to the constitution of IPNs but also to the swelling ratio of IPNs. There were interactions among the chains in the crosslinking networks and the interactions between COOH and OH increased with increasing PAA content. On the other hand, with increasing swelling ratio, the interaction space between the chains of networks became far and therefore interactions between the chains became weaker. So, the mechanical strength of IPN film decreased with the increase of the swelling ratio. These two effects on mechanical properties were opposite. As a result, tensile strength decreased with an increase of PAA content and this was because that the swelling ratio played a major role. But the results of the opposite effect made elongation at break have a maximum at 50% PAA. At the same time, mechanical property of GA = 0.5 wt % for PVA crosslinking was better than that of GA = 1.0 wt %. It was due to the higher degree crosslink decrease the chain mobility and hence tensile

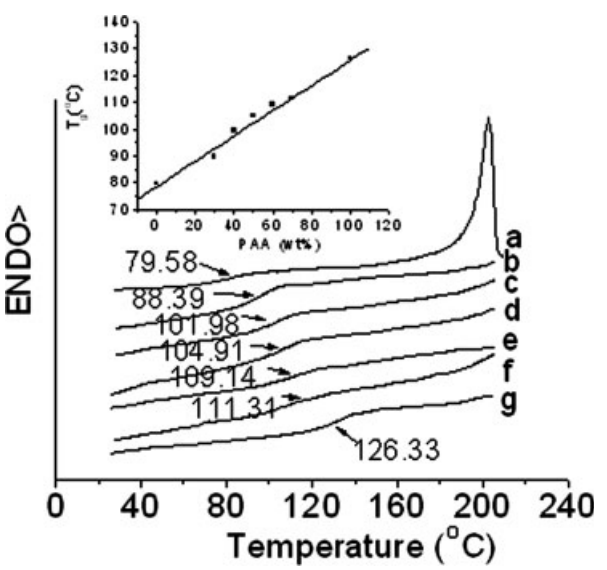

Figure 4 The DSC curves for PAA/PVA IPNs, PVA, and PAA. (a) For PVA, (b) for 30% PAA, (c) for 40% PAA, (d) for 50% PAA, (e) for 60% PAA, (f) for 70% PAA, and (g) for PAA.; and the T_g of the IPNs as a function of their composition. For all membranes, initiator and crosslinker are both 1.0 wt % PAA and GA is 1.0 wt % for PVA.

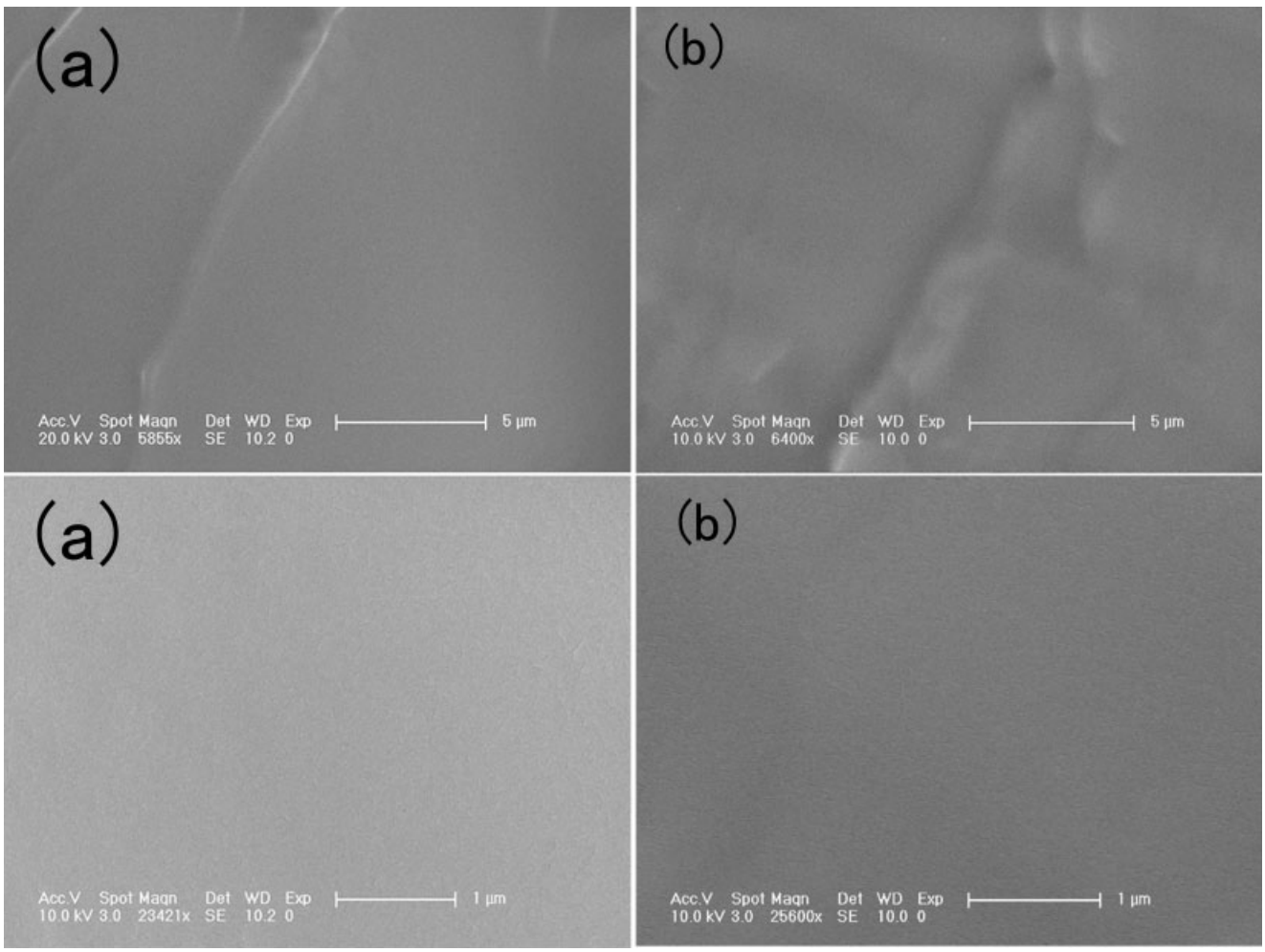

Figure 5 SEM photographs of the cross section of 70% (a), and 30% (b) PAA of IPNs.

strength decreased and more incline to elongation at higher crosslinking degree.

DSC analysis

From the T_g measurement, only a single glass transition temperature (T_g) for the IPN film was observed (Fig. 4), and this was attributed to the same network components in these IPN samples. The single T_g observed for each IPN sample also indicated that both IPN network components have excellent miscibility to each other in the IPN they formed. Figure 4 also exhibited the relationship of T_g values as a function of the weight ratio of the PAA component and T_gs of the IPNs increased with an increase in the PAA component ranged from 78°C of pure PVA to 126°C for pure PAA. Comparing to PVA/PAA blends system,[31] which was a significant deviation from the linear behavior, the T_g data of the IPN systems showed a very big difference that T_g had a linear relationship with network composition of IPN.

There are three main modes about the miscibility between two networks of an IPN by using the T_gs of an IPN sample.[14,32–36] When two networks of an IPN are incompatible, the IPN demonstrates two T_gs that correspond to those of their parent networks.[32] In this IPN sample, the interaction between the two networks could be neglected, leading to the fact that one network exerts less influence on the mobility of the other polymer network. As a result, each polymer network can retain their parent polymers. When two networks of an IPN exhibit partial compatibility, the IPN shows two T_gs that approach each other compared with those of the parent polymer.[37] When two networks of an IPN are compatible, the IPN possesses a single T_g.[33–36] In this IPN system, strong interactions exist between the two networks of this IPN.

In our IPN system, the single T_g data obtained should be hydrogen bond interaction between PVA and PAA.

Morphology studies

The IPN films were all transparent and smooth surface to the naked eyes. The scanning electron micrographs of the IPN films are shown in Figure 5. The

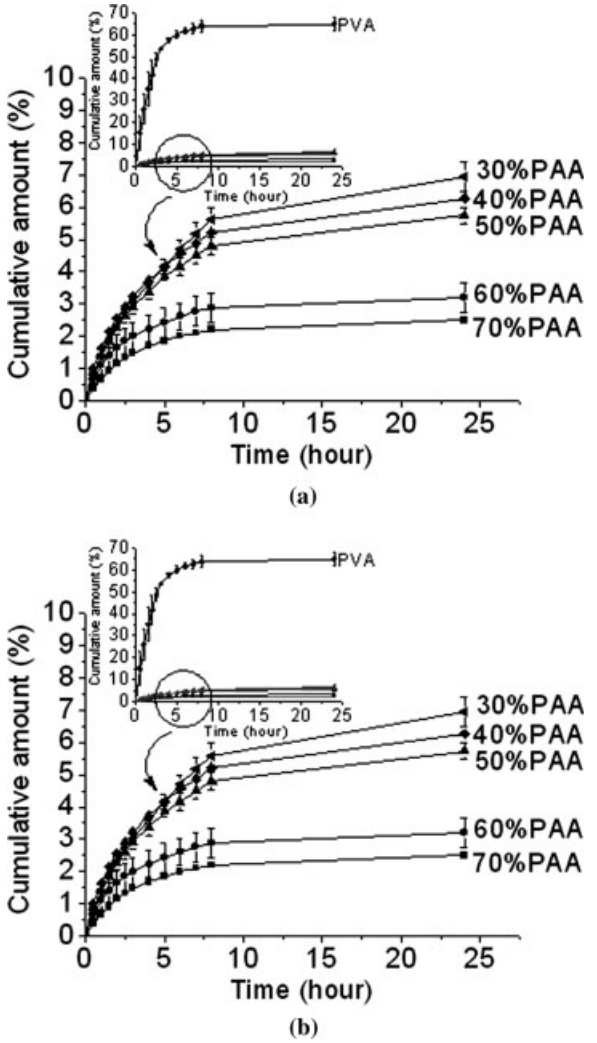

Figure 6 Crystal violet release profiles of PAA/PVA IPN films in 9 wt % NaCl solution at 25°C (a) and 37°C (b).

surface of films is very smooth, which indicated the good miscibility between the two polymers of IPNs (photographs not showed). The photographs of cross section observed a homogeneous structure, which also indicated the good compatibility and miscibility between PAA and PVA of IPNs (the crack was induced by elastic crack, not the representative of the structure in bulk). It confirmed the DSC results.

Drug release

The CV release profiles in 9 wt % NaCl solution at 25 and 37°C are shown in Figure 6. When compared with the high release rate for PVA due to simple adsorption between CV and PVA, for the PAA/PVA IPN films, the CV release exhibited sustained character. Because CV was cationic, when it was loaded in and release from the ionic IPN hydrogels, the electrostatic interaction may make a decisive effect. The charges of the drug and IPN hydrogel were different, and so the electrostatic attraction existed between them and the drug strongly binded in the IPN hydrogel matrix, and the release amount of the IPN film was lower.[38,39] Moreover, the higher the PAA content of IPN films, the stronger the interaction between the cationic CV and IPN networks; hence the release rate decreased in 9 wt % NaCl solution with PAA content increasing.

At the same time, at higher temperature, all the samples showed high release rate [shown in Fig. 6(b)]. It can be attributed to lower the electrostatic interaction between the drug and hydrogels[40] or faster diffusion rate of the drug from the matrix to external medium at higher temperature. But the interaction of the different charge between the drug and the hydrogels and its effect on the drug release from the IPNs in different external medium still need to be studied further.

CONCLUSIONS

A series of IPN films of PAA/PVA were successfully synthesized. The FTIR spectra analysis showed that the new interaction hydrogen bonds in IPN system were formed. Swelling properties of the films showed that the more the PAA content in the IPNs, the higher the swelling ratio in various medium. Swelling ratio decreased with increasing PVA crosslink degree. Mechanical characteristics were related to the composition and swelling ratio of the IPN films. Moreover, mechanical property of GA = 0.5% for PVA crosslinking was better than that of GA = 1.0%. A single glass transition temperature (T_g) displayed a linear relationship with network composition. SEM photograph exhibited a homogeneous structure, which indicated the good compatibility and miscibility between PAA and PVA. Potential application of the IPN films in controlled drug delivery was also examined. The release rate of the drug decrease with increasing PAA content and was higher at 37°C than that at 25°C in 9% NaCl solution. But the interaction of the different charge between the drug and the hydrogels and its effect on the drug release from the IPNs in different external medium still need to be studied further.

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