

# Release of Salicylic Acid through Poly(vinyl alcohol)/Poly(vinyl pyrrolidone) and Poly(vinyl alcohol-g-N-vinyl-2-pyrrolidone) Membranes

Oya Şanlı, Emel Orhan, Gülsen Asman

Gazi Üniversitesi, Fen Edebiyat Fakültesi, Kimya Bölümü, 06500 Teknikokullar, Ankara, Turkey

Received 7 November 2005; accepted 26 February 2006

DOI 10.1002/app.24453

Published online in Wiley InterScience (www.interscience.wiley.com).

**ABSTRACT:** A controlled release profile of salicylic acid (SA) for transdermal administration has been developed. Poly(vinyl alcohol) (PVA) and Poly(vinyl alcohol)/Poly(vinyl pyrrolidone) (PVP) blended preparations were used to prepare the membranes by solvent-casting technique. The release of the drug from the membranes was evaluated at *in vitro* conditions. The effects of PVA/PVP (v/v) ratio, pH, SA concentration and temperature were investigated. 60/40 (v/v) PVA/PVP ratio was found to be the best ratio for the SA release. Increase in pH and temperature

was observed to increase the transport of SA. Instead of blending PVA with PVP, N-Vinyl-2-pyrrolidone (VP) was grafted onto the PVA and the delivery performance for SA was compared with that of the blended PVA/PVP membranes. Grafted membranes gave higher transport percentages than the blended membranes. © 2006 Wiley Periodicals, Inc. *J Appl Polym Sci* 102: 1244–1253, 2006

**Key words:** salicylic acid; membrane; drug delivery systems; transdermal; blends

## INTRODUCTION

In the rapidly changing scientific world, scientists try to synthesize new molecules to reduce the problems of medicines and create new opportunities for treating and curing diseases. However these types of studies are time-consuming and are not economical. The pharmaceutical industry has encountered these problems with various drugs and methods. At present the most common form of delivery is via the oral route. Although this has the notable advantage of easy administration, it also has significant drawbacks namely poor bioavailability due to hepatic metabolism and the tendency to produce rapid blood level spikes (both high and low), leading to a need for high or frequent dosing, which can be both cost prohibitive and inconvenient. Another method utilized in drug delivery is the systems that deliver the drugs through the skin into the bloodstream, making them easy to administer. In transdermal drug delivery, improved bioavailability, more uniform plasma levels, longer duration of action resulting in a reduction in dosing frequency, reduced side effects and improved therapy due to maintenance of plasma levels up to the end of the dosing interval, and patient compliance could be possible.

Polymers are the backbone of the transdermal drug delivery systems and a specialized polymer system provides a vehicle for releasing active drug chemistries from device surfaces. The drug chemistries can be activated singularly or as “drug cocktails” designed for multiple indications including antibiotics, antimicrobials, antithrombogenic, antirestenosis, anti-inflammatory, anticancer, heparin complexes, etc.

Polyvinyl alcohol (PVA), which is a water soluble polyhydroxy polymer, is one of the widely used synthetic polymers for a variety of medical applications<sup>1</sup> because of easy preparation, excellent chemical resistance, and physical properties.<sup>2</sup> But it has poor stability in water because of its highly hydrophilic character. Therefore, to overcome this problem PVA should be insolubilized by copolymerization,<sup>3</sup> grafting,<sup>4,5</sup> crosslinking,<sup>6–10</sup> and blending.<sup>11</sup> These processes may lead a decrease in the hydrophilic character of PVA. Because of this reason these processes should be carried out in the presence of hydrophilic polymers. PVP is one of the hydrophilic, biocompatible polymer and it is used in many biomedical applications<sup>2,12,13</sup> and separation processes to increase the hydrophilic character of the blended polymeric materials.<sup>14,15</sup> An important factor in the development of new materials based on polymeric blends is the miscibility between the polymers in the mixture, because the degree of miscibility is directly related to the final properties of polymeric blends.<sup>16</sup> There are many studies related with the miscibility of PVA and PVP.<sup>14,15,17–23</sup> Lu et al.<sup>24</sup> and Ping et al.<sup>15</sup> reported that

Correspondence to: O. Şanlı (osanli@gazi.edu.tr).  
Contract grant sponsor: Gazi University.

PVA and PVP are miscible in any proportions in amorphous zones of the blends because of the hydrogen bonds between donor groups in PVA and acceptor groups in PVP. Ping et al.<sup>15</sup> also have determined that the aqueous solutions of PVA and PVP appear to be miscible in the whole composition range according to DSC results. Cassu and Felisberti<sup>22</sup> studied the miscibility of PVA and PVP, for different degrees of hydrolysis for PVA and for PVP of different molecular weights, by thermal analysis. They concluded that PVA and PVP are miscible at every composition. Lin et al.<sup>21</sup> have studied the miscibility of PVA/PVP blends by DSC, FTIR, and X-ray photoelectron spectroscopy (XPS). Lewandowska<sup>25</sup> studied the polymer/polymer miscibility of PVA/PVP by using viscosity measurements of dilute solutions of blend, in addition to DSC and FTIR measurements.

SA is an active component of aspirin and the regular use of aspirin by adults appears to reduce the risk of many diseases such as colon cancer, lung cancer, breast cancer, Alzheimer and heart diseases, etc. However it has the drawback of producing dyspepsia and gastrointestinal problems. One way to overcome these drawbacks is to use transdermal route; however there is a limited number of studies related with the transdermal usage of SA in the literature.<sup>26-32</sup>

Smith and Irwin<sup>27</sup> tried to investigate SA permeation through excised human skin (HS) and silastic rubber (SR) to assess the influence of a range of absorption enhancers on the transport of SA with an without a transmembrane pH-gradient.

Ishikawa et al.<sup>29</sup> studied the enhancing effect of switching iontophoresis on transdermal absorption and permeability of phtalic acid (PA), benzoic acid (BA), and SA for skin.

Gabboun et al.<sup>31</sup> studied the release of SA, diclofenac diethylamine, and diclofenac sodium from lyotropic structured systems across mid-dorsal hairless rat skin into aqueous buffer solutions.

Walkow and McGinity<sup>32</sup> studied the effect of physicochemical properties on the *in vitro* diffusion of salicylic acid through cellulose, dimethyl polysiloxane membranes, and pig skin into a receptor phase of aqueous glycol, water, and buffer solutions.

In this study the controlled delivery of SA from PVA/PVP membranes were studied. The effect of PVA/PVP ratio, pH, concentration of SA, and the temperature on the release of SA were investigated. Additionally the effect of grafting of *N*-vinyl-2-pyrrolidone onto PVA, instead of blending PVA with PVP, was searched.

## EXPERIMENTAL

### Materials

PVA ( $\bar{M}_w = 72,000$  g/mol, degree of saponification > 98%), PVP ( $\bar{M}_w = 40,000$  g/mol), *N*-vinyl-2-pyrro-

lidone (VP) ( $M_w = 182.14$  g/mol;  $d = 1.043$  kg/L) and salicylic acid ( $M_w = 138.12$  g/mol) were supplied by Merck Chemicals, UK. Benzophenone was purchased from Fluka.  $\text{Na}_2\text{HPO}_4$ ,  $\text{NaH}_2\text{PO}_4$ ,  $\text{CH}_3\text{COONa}$ ,  $\text{CH}_3\text{COOH}$ ,  $\text{CH}_3\text{OH}$ , and  $\text{C}_3\text{H}_6\text{O}$  were all from Merck. All of the products were used as supplied.

### Synthesis of PVA-g-VP copolymer

PVA (7% w/v) and VP (1M) were put into a three necked UV-Cell (Helios G.R.E.125W, Helios Ital-quartz) equipped with a magnetic stirrer and  $\text{N}_2$  inlet. After the addition of benzophenone (0.1% (w/v), in ethanol) polymerization reaction was carried out for 6 h with UV light. At the end of this period grafted copolymer was precipitated in an excess amount of acetone and washed with methanol to remove the homopolymer and dried under vacuum.

### Preparation of PVA membranes

PVA membranes were prepared by using aqueous solution of PVA at a concentration of 7.0% (w/v). Predetermined amount of polymer solution was cast onto the petri dishes. After complete dryness, they were heat-treated at 100°C for 75 min and the prepared membranes were preserved in buffer solutions till use.

### Preparation of PVA/PVP membranes

Membranes were prepared by using homogenous mixtures of PVA and PVP aqueous solutions at a concentration of 7.0% (w/v). Different amounts of PVA and PVP solutions (PVA/PVP (v/v): 90/10, 80/20, 70/30, 60/40) were mixed at room temperature. After being stirred for 1 day, the homogenous polymer solutions were cast onto petri dishes (4.5 in diameter) and then heat-treated as in PVA membranes. Details of PVA and PVA/PVP membranes were given in Table I.

### Preparation of PVA-g-VP membranes

Membranes were cast from the 2% (w/v) copolymer solutions (in 50% (v/v) acetone-water) and heat-treated as stated previously.

TABLE I  
PVA/PVP (v/v) Ratios in PVA/PVP Membranes

Membrane	PVA/PVP (v/v)
PVA	100/0
PVP-10	90/10
PVP-20	80/20
PVP-30	70/30
PVP-40	60/40

## Apparatus and measurements

### Infrared analysis

Infrared spectra of PVA/PVP and PVA-g-VP membranes were measured with Fourier Transform Infrared (FT-IR) Spectrometer of Unicam, Mattson 1000.

### Intrinsic viscosity measurements

Viscosity measurements were done by using Ubbelohde type viscometer at 25°C. Intrinsic viscosities of the polymer solutions were determined by using Huggins equation.

### Swelling studies

Swelling degrees % (SD%) of the membranes were computed by using

$$SD\% = \frac{W - W_0}{W_0} \times 100 \quad (1)$$

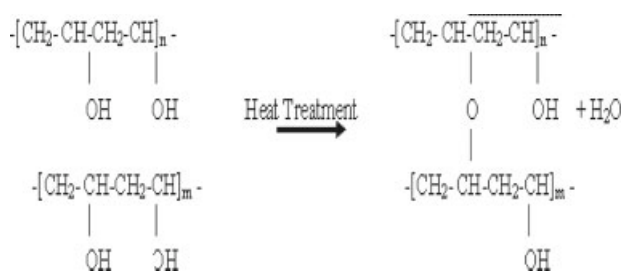
where,  $W$  and  $W_0$  are the wet and dry masses of the membranes, respectively.

### Scanning electron microscope (SEM) studies

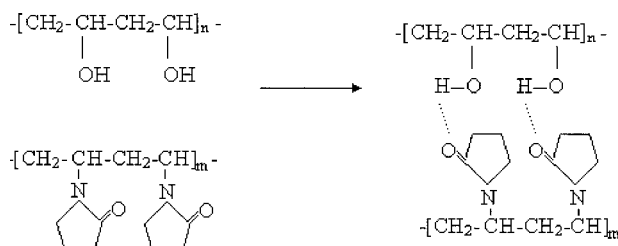
For SEM analysis the dried membranes were sputtered with gold in vacuum before viewing under the microscope (Model JEOL, JEM-100CXII).

### Permeation experiments

Permeation experiments were carried out at  $(37 \pm 1)^\circ\text{C}$  by using Franz Diffusion Cell. 3 mL of 2 mg/mL salicylic acid solution at different pH values (pH = 2.10–7.40) was placed into the upper compartment of the cell, a phosphate (pH = 7.4) and an acetate (pH = 2.1–5.0) buffer solutions were placed into the lower part at desired pH value. The lower compartment of the cell was stirred magnetically for uniform composition during the permeation. The receiver solution was sampled periodically and an equal volume of the buffer was added after each sampling.



Scheme 1



Scheme 2

The analysis of the samples was carried out spectrophotometrically at 298 nm by using Unicam UV2-100 UV-Vis Spectrophotometer. All of the data points are the average of at least three experimental results. The experiments are fairly reproducible.

## RESULTS AND DISCUSSION

### Characterization of PVA/PVP membranes

PVA is a biocompatible, hydrophilic, chemically stable polymer and has good film-forming ability. But it has poor stability in aqueous solutions. In this study heat treatment was applied to PVA membranes to prevent their solubility by crosslinking (Scheme 1).

However this process decreases the hydrophilic character of PVA membranes. To increase the hydrophilicity of the PVA membranes, PVA was blended with a hydrophilic biocompatible polymer PVP (Scheme 2).

PVA and PVP are perfectly compatible and miscible polymers via the hydrogen bond interactions between the  $-\text{CO}$  groups of PVP and  $-\text{OH}$  groups in PVA, in the amorphous zones of the blends, as given in Scheme 2.<sup>15,24</sup> FTIR spectroscopy is very sensitive to the formation of hydrogen bond ( $\text{XH}\dots\text{Y}$ ).<sup>33</sup> Figure 1 shows the IR spectra of the blend films. The strong absorption peak at  $1099\text{ cm}^{-1}$  has been assigned to the  $\text{C}-\text{O}$  in stretching mode for PVA and the bands observed at  $1333\text{ cm}^{-1}$  have been attributed to combination frequencies of  $(\text{CH} + \text{OH})$ .<sup>34</sup> As it is seen from the spectra of the blended membranes the change in the intensity of the peak around  $1099\text{ cm}^{-1}$  and  $1333\text{ cm}^{-1}$  attributed to the  $\text{CO}\dots\text{HO}$  hydrogen bond in PVA/PVP blend. The peaks that were observed at around  $3400\text{ cm}^{-1}$  and  $632\text{ cm}^{-1}$  arises from  $\text{O}-\text{H}$  stretching frequency, indicating the frequency of hydroxyl groups.<sup>34</sup> As it is seen from Figure 1 decrease in the intensity of  $\text{O}-\text{H}$  peaks at  $632\text{ cm}^{-1}$  supports the use of free  $-\text{OH}$  groups for  $\text{CO}\dots\text{HO}$  hydrogen bonding.

In Table II, elemental analysis of PVA/PVP membranes that were prepared from the polymer solutions of different PVA/PVP ratios were given. From Table II it is clearly seen that, as the amount of PVP in PVA-PVP volume solution increases, the amount

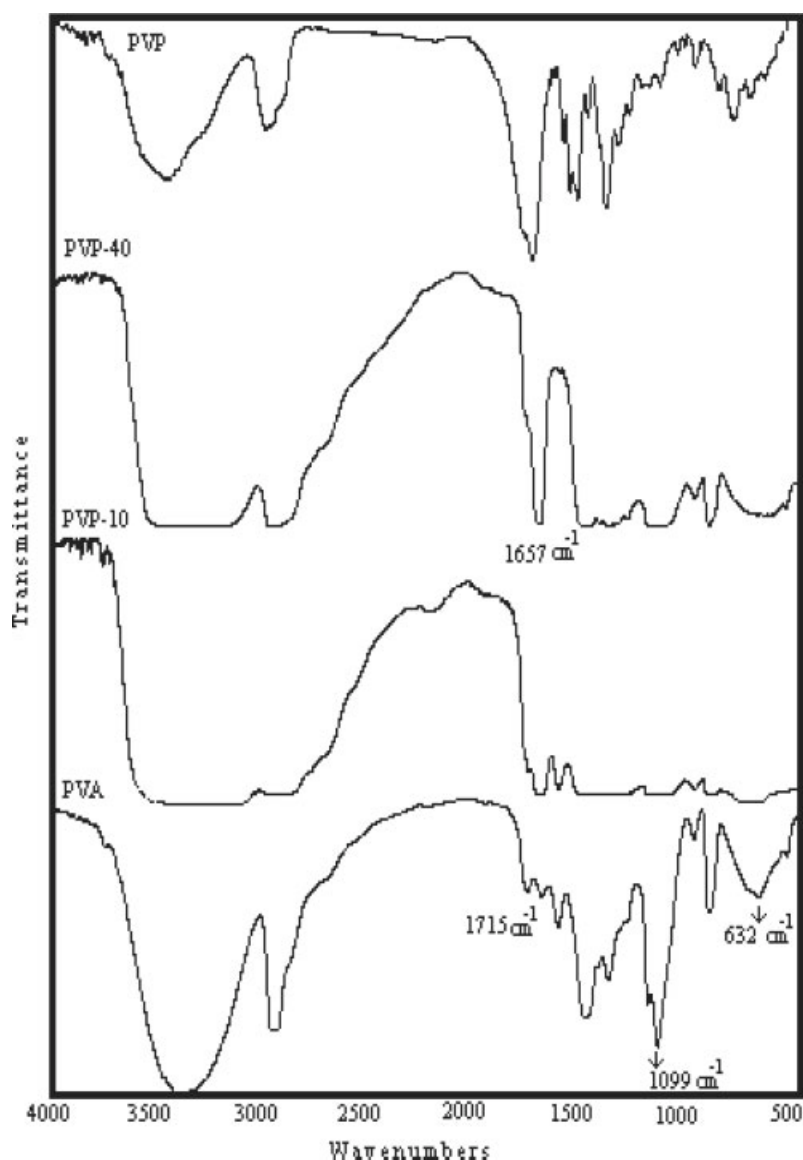


Figure 1 FTIR spectrum of PVA and PVA/PVP membranes.

of the PVP present in the crosslinked PVA/PVP membrane increases too.

In Table II SD% values of PVA/PVP membranes were also given together with the N% values that correspond to the pyrrolidone groups in PVP. It is clearly understood from the table that the hydrophilic character of the PVA/PVP membranes increases with an increase in the amount of PVP of the membrane material.

In Figures 2 and 3 SEM microfilms of the PVA and PVA/PVP membranes were given. As it is reflected from the figures, both the membranes are homogenous and nonporous.

#### Characterization of PVA-g-VP membranes

FTIR spectrum of the membranes were presented in Figure 4. The presence of VP in the copolymer was

determined from the characteristic bands at  $1660\text{ cm}^{-1}$  correspond to a mixed mode of carbonyl group stretch and  $-\text{N}-\text{C}$  stretch vibrations.

To determine the composition of the copolymer elemental analysis of the synthesized copolymer were done and the percentage of VP in the copolymer was found to be as 6.50%.

TABLE II  
N% and SD% Values of PVA and PVA/PVP Membranes

Membrane	N% (w/w) (in the membrane)	N% (w/w) (in the solution)	SD%
PVA	—	—	282.30
PVP-10	1.05	1.26	300.20
PVP-20	2.32	2.52	321.60
PVP-30	3.50	3.78	343.20
PVP-40	4.46	5.04	357.00

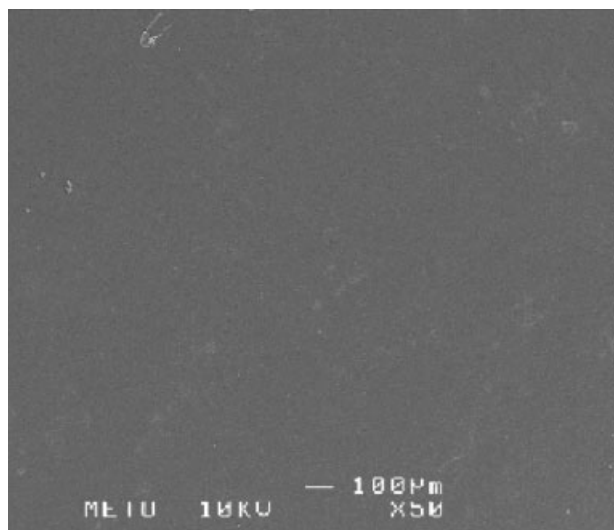


Figure 2 SEM micrograph of PVA membranes ( $\times 50$ ).

From the viscometric measurements intrinsic viscosities of PVA and PVA-g-VP were determined and given in Table III. The viscosity of the copolymer were found to be greater than that of PVA, which may be taken as an indication of the grafting of VP onto PVA.

SEM microfilm of the PVA-g-VP at  $\times 50$  magnification was given in Figure 5. As it is reflected from the figure that PVA-g-VP membranes were also homogeneous dense membranes and there are no detectible pores on the film surfaces similar to PVA/PVP membranes.

#### Effect of PVA/PVP ratio on permeability

Permeation behavior of PVA and PVA/PVP membranes with different PVA/PVP ratios were studied at  $(37 \pm 1)^\circ\text{C}$  and were given in Figure 6, and the permeability coefficients ( $P$ ), which is a measure of the permeation ability of a membrane, were deter-

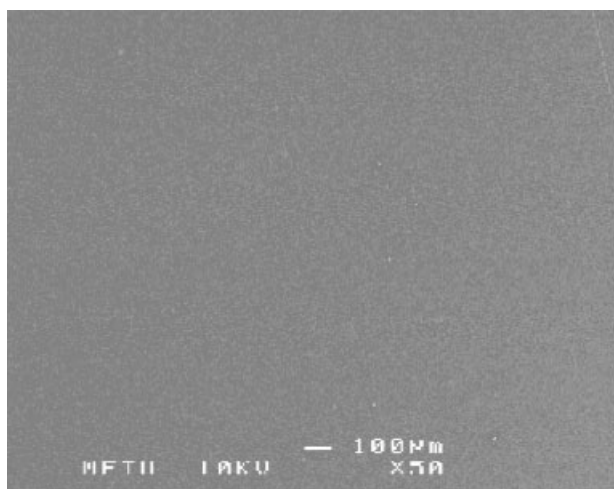


Figure 3 SEM micrograph of PVP-40 membranes ( $\times 50$ ).

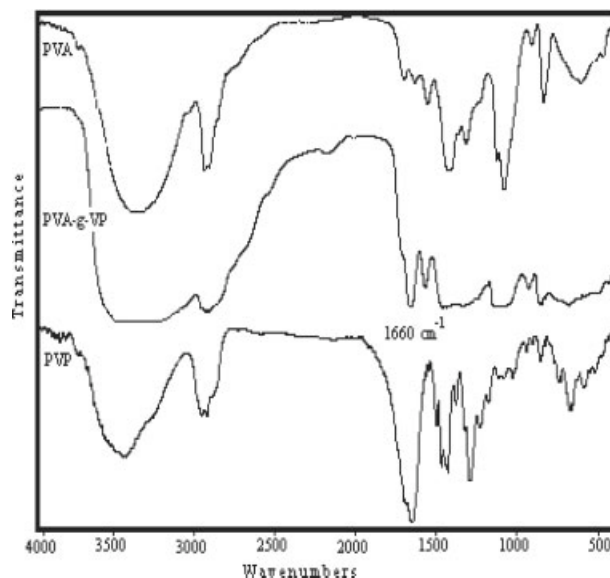


Figure 4 FTIR spectrum of PVP, PVA-g-VP, and PVA.

mined from the slope of  $Q_t$  versus  $t$  in steady state according to the eq. 2<sup>35,36</sup> and the results were presented in Table IV.

$$Q_t = \frac{PC_0 D}{L} \left( t - \frac{L^2}{6D} \right) \quad (2)$$

Where  $C_0$  is the concentration of the donor side of the cell,  $D$  is the diffusion coefficient,  $L$  is the thickness of the membrane,  $t$  is the time and  $Q_t$  is the amount of drug diffused through the unit area at time  $t$ .

From the results it is clear that the presence of PVP increased the permeability of the membranes and the % release of SA. At the beginning there is no detectible difference between the % release values of the membranes up to 4 h in Figure 6 because of the swelling equilibrium of the membranes, but after that period %release of SA increases as the PVP content of the membrane increases.

Increase in the release% of the SA with PVP can be explained by the hydrophilic character of PVP. As it is seen in Table II, increase in the amount of PVP in the membrane increases the swelling degrees of the PVA/PVP membranes, indicating the hydrophilic character of the membranes. When the degree of swelling increases, amorphous regions produce free volumes that are suitable for diffusion of the drug.

TABLE III  
Results of Viscometric Measurements  
of PVA and PVA-g-VP

Polymer	$[\eta]$ ( $\text{cm}^3/\text{g}$ )
PVA	0.9870
PVA-g-VP	1.2819

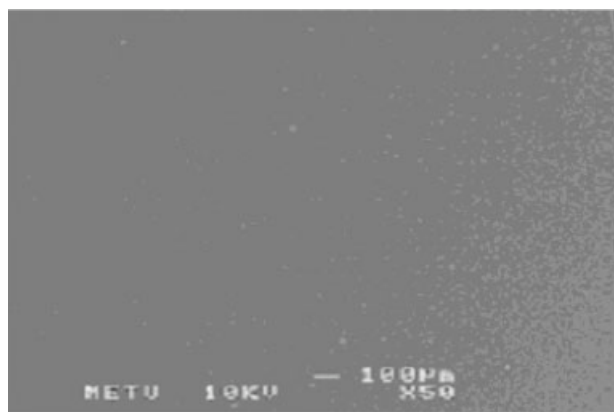


Figure 5 SEM micrograph of PVA-g-VP membranes ( $\times 50$ ).

Therefore permeation coefficient and the % release of SA increase with the PVP content of the membranes. Since the % release value (Fig. 6) and the permeability coefficient were found to be slightly higher for PVP-40 blend membranes. PVP-40 membranes were used in the rest of the study.

#### Effect of SA concentration and pH of donor solution on the release of SA

In this part of the study the effect of pH and drug concentration on the release of SA were investigated. For

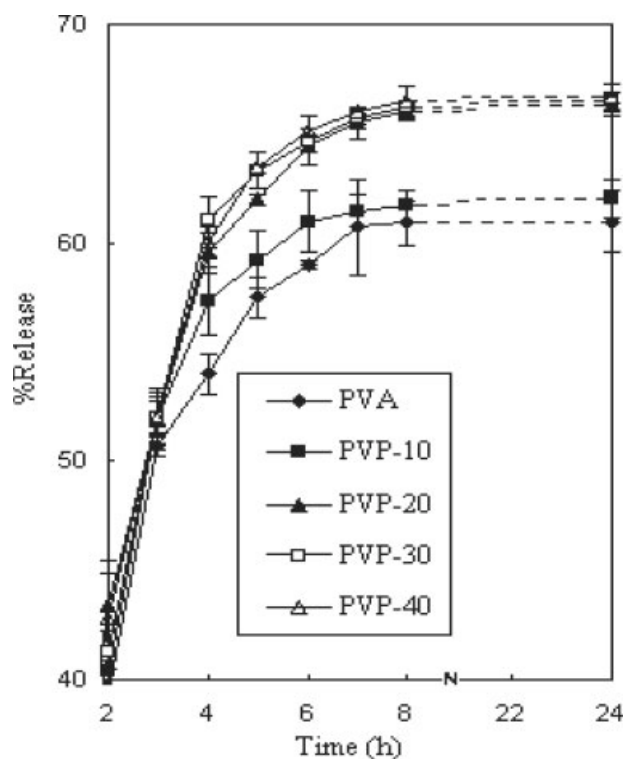


Figure 6 Effect of PVP on the % release of SA ( $t = (37 \pm 1)^\circ\text{C}$ ,  $\text{pH} = 7.4$ ).

TABLE IV  
Permeability Coefficients of PVA  
and PVA/PVP Membranes

Membrane	$P$ ( $10^4 \text{ cm}^2/\text{h}$ )
PVA	3.38
PVP-10	3.51
PVP-20	3.56
PVP-30	3.58
PVP-40	3.60

this purpose 2.0 mg/mL and saturated SA solutions were prepared at pH of 2.1–7.4 and the pH of the acceptor compartment was kept constant at 7.4. The results of the permeation studies for both unsaturated and saturated solutions by using PVP-40 membranes were given in Figures 7 and 8, respectively.

As it is reflected from the figures, it can be seen that increase in pH of the donor compartment increases the release of the SA for both type of SA solutions. For the weak acids, the relationship between pH and solubility of ionisable compounds can be derived from Handerson–Hasselbalch equation.<sup>27</sup> According to this equation, the overall solubility ( $S$ ) of a weak acid can be expressed as  $S = S_0 \frac{([\text{H}_3\text{O}^+] + K_a)}{[\text{H}_3\text{O}^+]}$ , where  $S_0$  is the solubility of unionized species. For saturated suspensions,  $S_0$  is constant and independent of pH and only the degree of ionization can be changed with pH. SA is also a weak acid and pH affects the ionization of SA in a

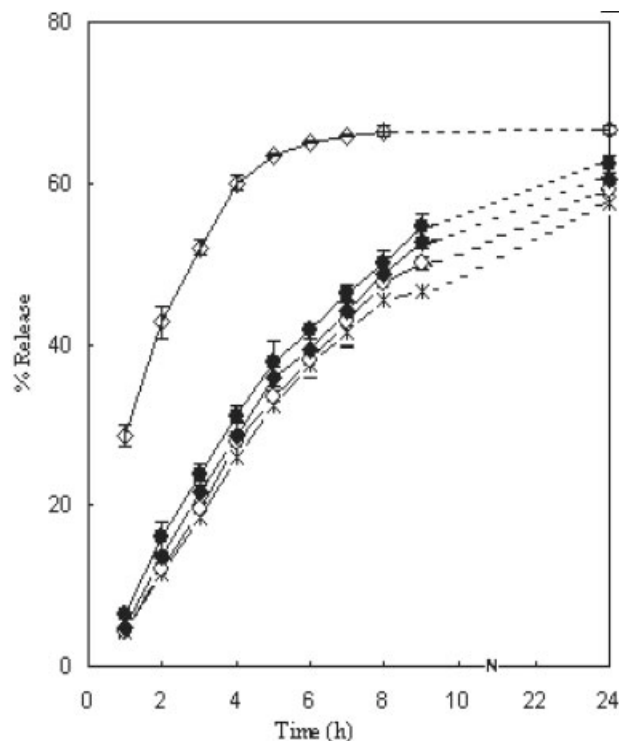
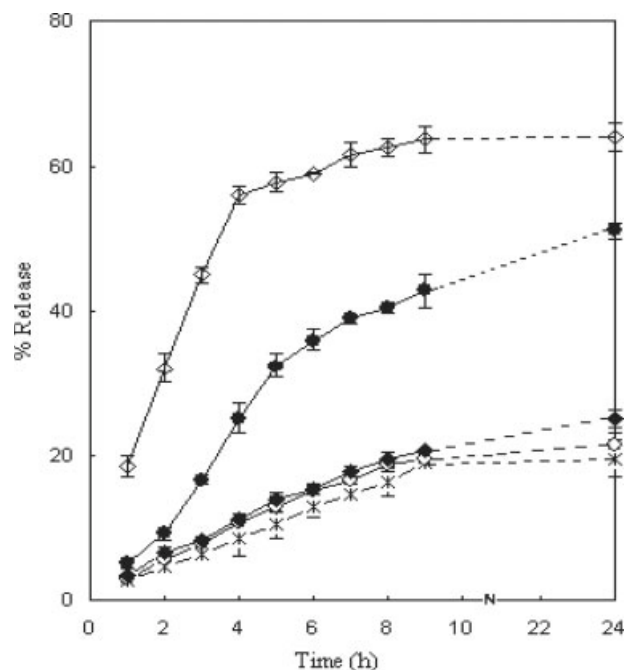


Figure 7 Effect of pH on the % release of SA through PVP-40 membranes for 2.00 mg/mL SA solutions. \*,  $\text{pH} = 2.10$ ; O,  $\text{pH} = 3.50$ ; ◆,  $\text{pH} = 4.30$ ; ●,  $\text{pH} = 5.00$ ; ◇,  $\text{pH} = 7.4$ .



**Figure 8** Effect of pH on the % release of SA through PVP-40 membranes for saturated SA solutions. \*, pH = 2.10; O, pH = 3.50; ◆, pH = 4.30; ●, pH = 5.00; ◇, pH = 7.4.

way that explained earlier. Ionization % of unsaturated and saturated SA solutions for different pH values were calculated from the Henderson–Hasselbalch equation [ $\text{p}K_a(\text{SA}) = 2.9$ ]. They were presented in Table V. From the Table it is clearly seen that as the pH of SA solutions increases, the percent ionization increases too. Permeation coefficients were calculated and given in Table VI. From the Table VI it could be said that ionization of SA plays an important role in permeability. This may be caused from the interaction of  $-\text{COOH}$  groups in ionized SA with the  $-\text{N}$  groups in PVP via hydrogen bonding at the membrane surface at high pH values.<sup>37</sup>

Additionally when the pH of the donor solution increases PVP interacts with  $-\text{OH}$  groups by hydrogen bonding<sup>15,22,24</sup> leading to increase in the SD values (Table VII). When the SD values of the membrane increases free volumes that were responsible for the diffusion of SA through the polymeric membrane increases too. This may be an additional

**TABLE V**  
Percent Ionization of Saturated and Unsaturated SA Solutions at Different pH Values

pH	Ionization % (Std. SA)	Ionization % (2.00 mg/mL SA)
2.10	0.47	9.00
3.50	11.19	72.00
4.30	44.57	94.00
5.00	91.46	99.00
7.40	99.98	99.99

**TABLE VI**  
Permeability Coefficients of PVP-40 Membranes at Different pH Values

pH	Solubility of SA (mg/mL)	P ( $10^4 \text{ cm}^2/\text{h}$ ) (std. SA solution)	P ( $10^4 \text{ cm}^2/\text{h}$ ) (2 mg/mL SA solution)
2.10	5.00	0.71	1.95
3.50	5.20	0.74	2.05
4.30	5.30	0.76	2.08
5.00	14.03	2.48	2.08
7.40	30.14	4.23	3.60

reason for getting high % release and permeation coefficients at high pH values.

Walkow and McGinity<sup>32</sup> studied the effect of physicochemical properties on the *in vitro* diffusion of SA through dimethylglycol polysiloxane and cellulose membranes additional to pigskin. They have determined that cellulose membranes have greater permeability with a permeability coefficient of  $74.28 \times 10^{-4} \text{ cm}^2/\text{h}$  by using methyl glucose ether as a vehicle at pH 7.4.

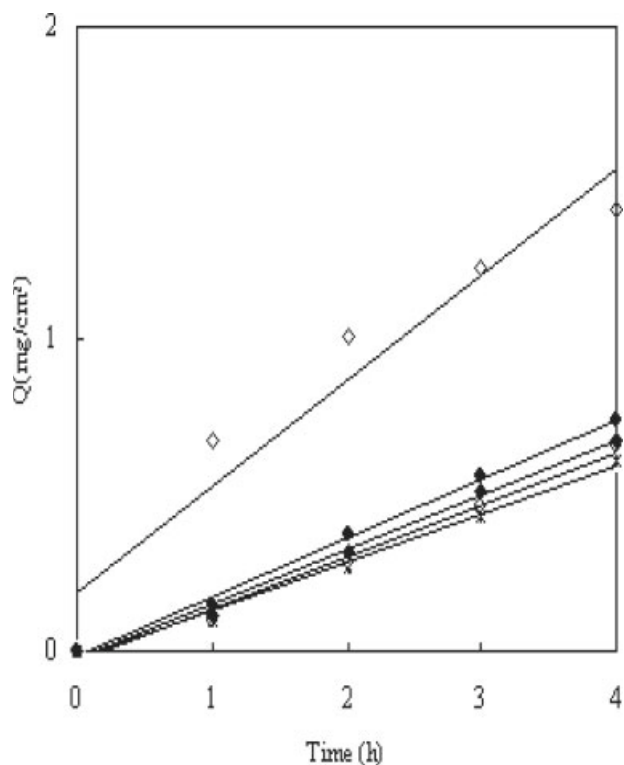
Figures 9 and 10 show the dependence of  $Q_t$  versus  $t$  for unsaturated and saturated SA solutions, respectively. If the linear plot of  $Q_t$  versus  $t$  is extrapolated to  $Q_t$  axis, the resulting intercept includes  $(L^2/6D)$  the term called as the lag time (eq. 2).<sup>35,36</sup> As it is seen from the figures there was no occurrence of lag time especially below the pH of 7.4 at which high ionization percentages were obtained for SA. The absence of a lag time indicates that, for these experiments, the equilibrium seemed to be instantaneously established. This may be attributed to the use of swollen membranes since they were preserved in buffer solutions till use. Because the percent ionization of SA is high at pH 7.4, the presence of lag time may be explained by the interaction of salicylate ions with the membrane material at this pH.

#### Effect of pH of acceptor solution on the release of SA

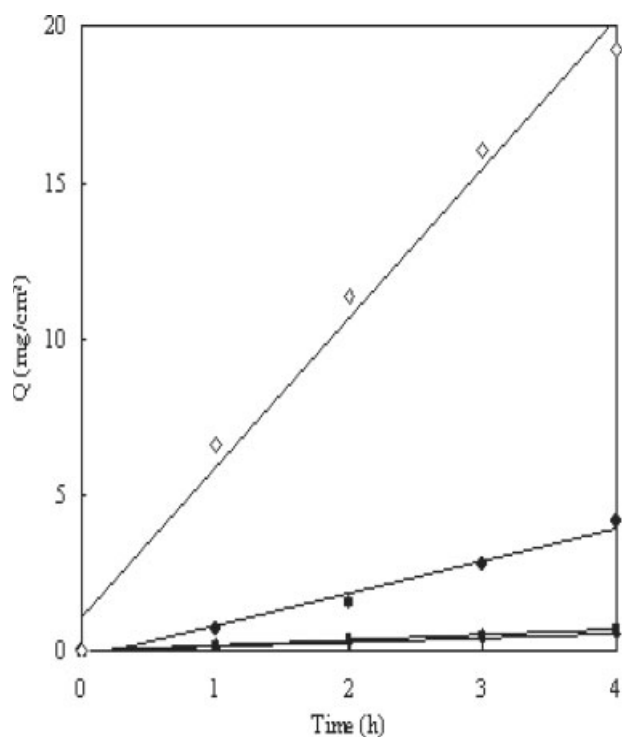
To determine the effect of the pH of the acceptor solution, the pH of the donor and acceptor solutions were adjusted to the same pH values (2.1–7.4) and the concentrations of the SA solutions were kept constant at 2.0 mg/mL. The results were given in Figure 11.

**TABLE VII**  
SD Values of PVP-40 Membranes at Different pH Values

pH	SD%
2.10	252.10
3.50	273.95
4.30	304.90
5.00	316.30
7.40	357.00



**Figure 9**  $Q-t$  diagram for the unsaturated SA solutions at 2.00 mg/mL. \*, pH = 2.10; ○, pH = 3.50; ◆, pH = 4.30; ●, pH = 5.00; ◇, pH = 7.4.



**Figure 10**  $Q-t$  diagram for the saturated SA solutions. \*, pH = 2.10; ○, pH = 3.50; ◆, pH = 4.30; ●, pH = 5.00; ◇, pH = 7.4.

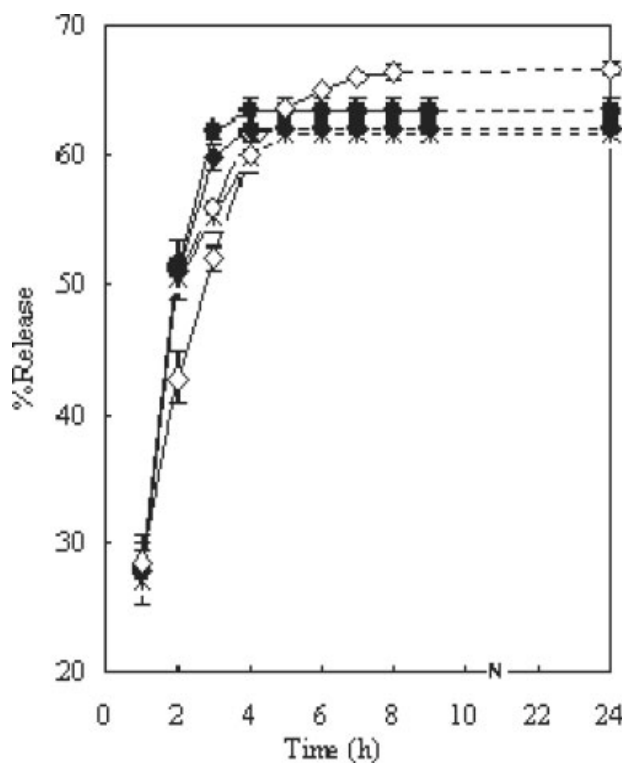
As it is seen from the figure, the results were similar to that were obtained for acceptor compartment pH of 7.4. Therefore, it could be said that the pH of acceptor solution does not affect very much the release characteristics of SA solutions.

**Release of SA through PVA-g-VP membranes**

The release characteristics of 2.00 mg/mL of SA solutions through PVA-g-VP membranes were studied at pH 7.4 for comparison. PVP-6.5 membranes were prepared by taking the PVA/PVP volume ratio as 93.5/6.5 and the results were given in Figure 12.

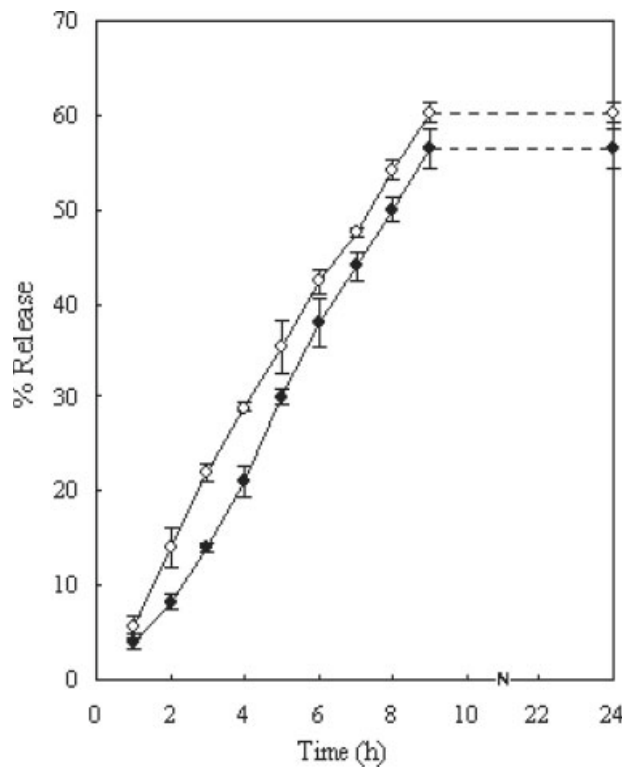
As it is seen from the figure, there is no great difference between the release percentages of SA from PVA-g-VP membranes and from PVP-6.5 membranes. In Table VIII elemental analysis of PVA-g-VP and PVP-6.5 membranes were given together with the SD values and the permeability coefficients.

From the elemental analysis of the PVA-g-VP and PVP-6.5 membranes, it is seen that PVA-g-VP membranes contains greater amount of pyrrolidone groups than PVP-6.5 blend membranes that will affect the SD% value positively. This should be the reason of high permeability coefficients and release percentages of PVA-g-VP membranes than that of the PVP-6.5 membranes.



**Figure 11** Effect of pH of the acceptor compartment on the % release of SA. \*, pH = 2.10; ○, pH = 3.50; ◆, pH = 4.30; ●, pH = 5.00; ◇, pH = 7.4.





**Figure 12** Comparison of the release profiles of PVA-g-VP and PVP-6.5 membranes: ○, PVA-g-VP; ●, PVP-6.5.

The  $Q-t$  graphs of PVA-g-VP and PVP-6.5 membranes were given in Figure 13. It is clearly seen that small lag time is observed for both type of the membranes. The observed small-lag time shows that the equilibrium could be established easily.

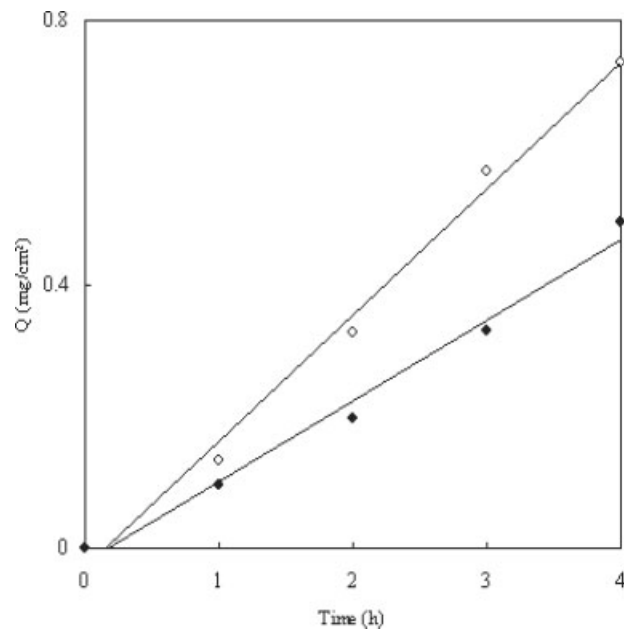
#### Effect of temperature on the release of salicylic acid

To investigate the effect of temperature on the permeation of salicylic acid, the release experiments were run at  $(32 \pm 1)^\circ\text{C}$  and  $(37 \pm 1)^\circ\text{C}$  by using 2.00 mg/mL SA solution at pH of 7.4. Figure 14 represents the results of permeation.

As it is seen from the figure temperature affects the permeation of SA. This can be explained by free volume theory.<sup>38</sup> According to this theory, the thermal motion of polymer chains in the amorphous regions randomly produces free volume. As the temperature increases, the frequency and the amplitude of the chain jumping increases and the resulting free volumes become larger for the diffusion of SA molecules, leading to high percentage release (Table IX).

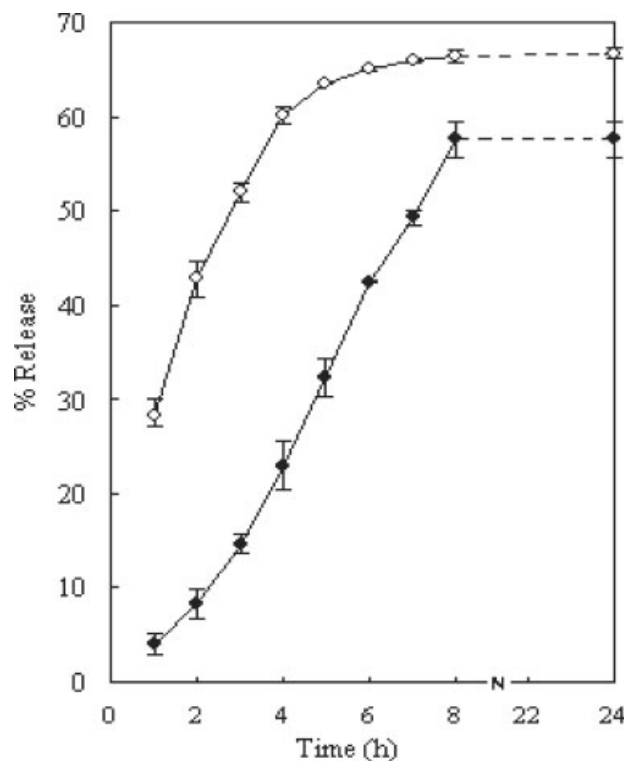
**TABLE VIII**  
Comparison of PVP-g-VP and PVP-6.5 Membranes

Membrane	SD%	N%	$P$ ( $10^4 \text{ cm}^2/\text{h}$ )
PVA-g-VP	289.00	0.82	2.52
PVP-6.50	285.00	0.78	2.43



**Figure 13**  $Q-t$  diagram for PVA-g-VP and PVP-6.5 membranes: ○, PVA-g-VP; ●, PVP-6.5.

Additionally increase in temperature increases the mobility of the permeants.<sup>39</sup> Therefore an interaction between the permeating particles and also with the membrane material decreases. This also accelerates the permeation positively, resulting high permeability coefficients (Table IX).



**Figure 14** Effect of temperature on the release of SA: ○,  $(37 \pm 1)^\circ\text{C}$ ; ●,  $(32 \pm 1)^\circ\text{C}$ .

**TABLE IX**  
The Change in SD and P Values of PVP-40 Membranes with Temperature

Temperature (°C)	SD%	P (10 <sup>4</sup> cm <sup>2</sup> /h)
37 ± 1	357.00	3.60
32 ± 1	266.40	2.68

Fitzpatrick and Corish<sup>40</sup> used cellulose membranes to release of SA. They determined that by using 0.1M SA solution 26% of SA was released at 310 K at the end of 24 h.

The release percentage for SA was found as 57.5% and 66.6% at (32 ± 1)°C and (37 ± 1)°C, respectively, in our study.

### CONCLUSIONS

The following conclusions may be drawn from this study

1. The presence of PVP increased the released amount of SA. Suitable PVA/PVP ratio was found to be as 60/40 (v/v) for PVA/PVP membranes.
2. % release of SA through PVA/PVP membranes and swelling degrees of the PVP-40 membranes increased with an increase in the pH of donor solution. The pH of the acceptor solution did not affect much the transfer of SA through PVP-40 membranes.
3. Grafting of PVA with VP is more effective than blending with PVP for the release of SA.
4. The increase in the temperature increased the transfer of SA. The release percentage for SA was found as 57.5% and 66.6% at (32 ± 1)°C and (37 ± 1)°C, respectively.

We are grateful to Gazi University Research Fund for the support of this study.

### References

1. Sreenivasan, K. J Appl Polym Sci 2004, 94, 651.
2. Martien, F. L. Encyclopedia of Polymer Science and Engineering, Vol. 17; Wiley: New York, 1986; p 167.
3. Lee, K. H.; Kim, H. K.; Rhim, J. W. J Appl Polym Sci 1995, 58, 1707.
4. Huang, R. Y. M.; Yeom, C. K. J Membr Sci 1991, 62, 59.
5. Nguyen, Q. T.; Essamri, A.; Schaezel, P.; Neel, J. Macromol Chem 1993, 194, 1157.
6. Oh, B. K.; Lee, Y. M. J Membr Sci 1996, 113, 183.
7. Xu, Y. F.; Huang, R. Y. M. J Appl Polym Sci 1988, 36, 1121.
8. Miyata, T.; Iwamoto T.; Uragami T. J Appl Polym Sci 1994, 51, 2007.
9. Nguyen, T. Q.; Essamri, A.; Clement R.; Neel, J. Makromol Chem 1987, 188, 1973.
10. Yeom, C. K.; Lee, K. H. J Appl Polym Sci 1996, 59, 1271.
11. Feng, X.; Huang, R. Y. M. J Membr Sci 1996, 109, 165.
12. Seabra, A. B.; Da Rocha, L. L.; Eberlin, M. N.; De Oliveira, M. G. J Pharm Sci 2005, 95, 994.
13. Luttinger, M.; Cooper, C. W. J Biomed Mater Res 1967, 1, 67.
14. Ping, Z.; Nguyen, Q. T.; Essamri, A.; Néel, J. Polym Adv Technol 1994, 5, 320.
15. Ping, Z.; Nguyen, Q. T.; Néel, J. Macromol Chem Phys 1994, 195, 2107.
16. Mano, V.; Silva, M. E. S. R. E.; Barbani, N.; Giusti, P. J Appl Polym Sci 2004, 92, 743.
17. Narayona, K. L.; Dasaradhu, Y.; Narasimha Rao, V. V. R. Polym Int 1994, 35, 315.
18. Nishio, Y.; Haratani, T.; Takahashi, T. J Appl Polym Sci Part B: Polym Phys 1990, 28, 355.
19. Eguiazabal, J. I.; Calahorra, E.; Cortazar, M.; Guzman, G. M. Makromol Chem 1986, 187, 2439.
20. Feng, H.; Feng, Z.; Shen, L. Polymer 1993, 34, 2516.
21. Lin, L.; Chan, Ch. M.; Weng, L. T. Polymer 1998, 39, 2355.
22. Cassu, S. N.; Felisberti, M. I. Polymer 1997, 38, 3907.
23. Cassu, S. N.; Felisberti, M. I. Polymer 1999, 40, 4845.
24. Lu, J.; Nguyen, Q.; Zhou, J.; Ping, Z. H. J Appl Polym Sci 2003, 89, 2808.
25. Lewandowska, K. Eur Polym J 2005, 41, 55.
26. Imanidis, G.; Helbing-Strausak, S.; Imboden, R.; Levenberger, H. J Controlled Release 1998, 51, 23.
27. Smith, J. C.; Irwin, W. J. Int J Pharm 2000, 210, 69.
28. Schmook, F. P.; Meingassner, J. G.; Billich, A. Int J Pharm 2001, 215, 51.
29. Ishikawa, O.; Kato, Y.; Onishi, H.; Nagai, T.; Machida, Y. Int J Pharm 2002, 249, 81.
30. Leveque, N.; Makki, S.; Hadgraft, J.; Humbert, P. Int J Pharm 2004, 269, 323.
31. Gabboun, N. H.; Najib, N. M.; Ibrahim, H. G.; Assaf, S. Int J Pharm 2001, 212, 73.
32. Walkow, J. C.; McGinity, J. W. Int J Pharm 1987, 35, 103.
33. He, Y.; Zhu, B.; Inoue, Y. Prog Polym Sci 2004, 29, 1021.
34. Kumar, G. N. H.; Rao, J. L.; Gopal, N. O.; Narashimulu, K. V.; Chakradhar, R. P. S.; Rajulu A. V. Polymer 2004, 45, 5407.
35. Şanlı, O.; Asman, G. J Appl Polym Sci 2004, 91, 72.
36. Rocha, A. N. L.; Dantas, T. N. C.; Fonseca, J. L. C.; Pereira, M. R. J Appl Polym Sci 2002, 84, 44.
37. Endo, T.; Numazawa, R.; Okawara, M. Die Makromol Chem 1971, 148, 205.
38. Huang, R. Y. M.; Yeom, C. K. J Membr Sci 1991, 58, 33.
39. Uragami, T.; Shinomiya, H. Macromol Chem 1991, 192, 2293.
40. Fitzpatrick, D.; Corish, J. Int J Pharm 2005, 301, 226.