The Diffusion and Bulk Properties of Polyurethane (PU)-Based Hydrophilic and Hydrophobic Membranes

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ABSTRACT: In this study, the diffusion characteristics of diclofenac-Na through hydrophobic and hydrophilic polyurethane (PU)-based membranes are investigated. Hydrophilic polymers are obtained by graft copolymerization of PU with acriylamide (AAm) and itaconic acid (IA). The membranes are prepared by a solvent-casting method and characterized by Fourier transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM) analysis. The diffusion measurements are performed using a diffusion cell for 10 h at 37°C. Permeability coefficients calculated from diffusion experiments are ~3 times higher in hydrophilic membranes than hydrophobic PU membranes. © 2002 Wiley Periodicals, Inc. J Appl Polym Sci 85: 193-198, 2002

Key words: polyurethane; acrylamide; itaconic acid; diclofenac-Na; membrane; diffusion; permeability coefficient; scanning electron microscopy

INTRODUCTION

The use of polymers as vehicles for controlled release of drugs is a young, vigorous field.[1–3] Polymers release drugs by four general mechanisms: diffusion, chemical control, solvent activation, and magnetism.[4] The most common mechanism is diffusion consisting of matrix or reservoir (membrane) systems. In the reservoir system, drug solution surrounded by a polymeric membrane is at saturated concentration to keep the release rate constant (zero-order release kinetics).[5,6]

The role of polyurethane (PU) as a material for biomedical prostheses has become increasingly important in recent years.[7,8] Nonthrombogenicity and reistance to biodegradation of PU has led to its use in both commercial and experimental blood-contacting applications; such as catheters, heart-assist pumps; and chambers for artificial hearts, and pacemaker wire lead insulation.[9,10] There are also several studies in the literature about drug release from PU-based membrane and matrix systems.[11]

Graft copolymerization often offers a possibility of incorporating diverse useful properties in conventional polymers. Consequently, the solubility characteristics and mechanical and physiochemical properties of the backbone polymers could be improved. Synthesis of graft copolymers of PU by free radical irradiation and anionic techniques have been widely reported.[12–15] As is known, PU is in hydrophobic character. Graft copolymerization with hydrophilic monomers, such as acrylic acid, acrylamide (AAm), itaconic acid (IA), etc., increases the hydrophilic character of PU materials. Graft copolymerization of IA and AAm are frequently performed in various studies.[16–18]

Diclofenac sodium (DCF-Na) is a nonsteroidal anti-inflammatory analgesic drug that is widely used in the treatment of rheumatic disorders. The pharmacokinetic performance of sustained-release formulations of DCF-Na have been studied

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in several reports.[19] It is important to develop a controlled-release system of DCF-Na to remove the gastrointestinal damage of usual therapeutic dosages.[20]

In our previous studies, bulk, surface, and diffusion properties and biocompatibilities of PU, polyhydroxyethylmethacrylate (PHEMA), and polyvinylchloride membranes were investigated in detail.[21–26]

The aim of this study is to investigate the DCF-Na release through a series of membranes prepared by graft copolymerization of PU with AAm and IA. Hydrophobic (PU) and hydrophilic (PU–PAAm, PU–PIA) polymers were chosen to determine the effect of hydrophilicity on the diffusion characteristics.

EXPERIMENTAL

Preparation of PU based membranes

To prepare the PU, PU–PAAm, and PU–PIA membranes, PU (®Pellethane, Up-John), AAm (Sigma), and IA (Sigma) were used. As is known, PU has a hydrophobic character opposite to that of PAAm and PIA. The PU membrane was prepared from 2.5 g/30 mL PU-dioxane solution by the classical solvent-casting method.[21–25] In this method, equal volumes of polymer solution were poured into the identical Petri dishes, which were left at room temperature until the solvent was completely evaporated, and then sunk into a waterbath to remove the membrane from the surface of Petri dishes.

Three types of PU–PAAm and three types of PU–PIA membranes were prepared by copolymerization of PU with AAm and IA monomers in 2.5 g/30 mL PU-dioxane solution, respectively.[17,18] The copolymerizations were carried out by adding the different amounts of monomer (from 0.75 to 1.75 g) and benzoylperoxide initiator (BO); from 0.025 to 0.050 g; (Aldrich) into the PU-dioxane solutions at 60°C. The mixture was sitirred for 24 h and cast into the Petri dishes, and the membranes were removed as already explained. The preparation conditions of membranes are presented in Table I.

Table I Preparation Conditions of Membranes in 30 mL of Dioxane

Membrane	PU (g)	AAm (g)	IA (g)	BO (g)
PU	2.5			
$(AAm)_1$	2.5	0.75		0.025
$(AAm)_2$	2.5	1.25		0.040
$(AAm)_3$	2.5	1.75		0.050
$(IA)_1$	2.5		0.75	0.025
$(IA)_2$	2.5		1.25	0.040
$(IA)_3$	2.5		1.75	0.050

The wet thicknesses of the membranes were measured with a micrometer by swelling them to constant thickness in distilled water at 37°C.

Diffusion Measurements

All experiments were performed with wet membranes for 10 h at 37°C using a glass diffusion cell. The effective membrane area was 19.62 cm^2. The left compartment of the cell was filled with 160 mL of DCF-Na solution of 6250 μg/mL (C'). An equal volume of water was poured into the right compartment. Both sides of the cell were mechanically stirred at a constant rate. The concentration of the DCF-Na (C'') that diffused from left to right through the membrane was measured at 1-h intervals by ultraviolet (UV) spectrophotometry (UNICAM UV 2-100). The UV measurements were performed at 276 nm.[27]

If we assume that C' is the initial concentration of the drug solution in the left compartment of the diffusion cell and that C'' is the drug concentration in the right compartment at a reached time t, then the flux of the solute, J (mol/cm^2.s) will be:

$$J = \frac{D(C' - C'')}{x} \tag{1}$$

where D is the diffusion coefficient (cm^2/s) at the given temperature and x is the membrane thick-

Table II Thicknesses and Swelling Percentage of the Membranes

Membrane	PU	$(AAm)_1$	$(AAm)_2$	$(AAm)_3$	$(IA)_1$	$(IA)_2$	$(IA)_3$
Thickness (μm)	52.8	71.4	83.2	130.0	87.6	114.2	122.4
Swelling (%)	2.1	7.8	15.4	27.6	3.8	6.6	25.7

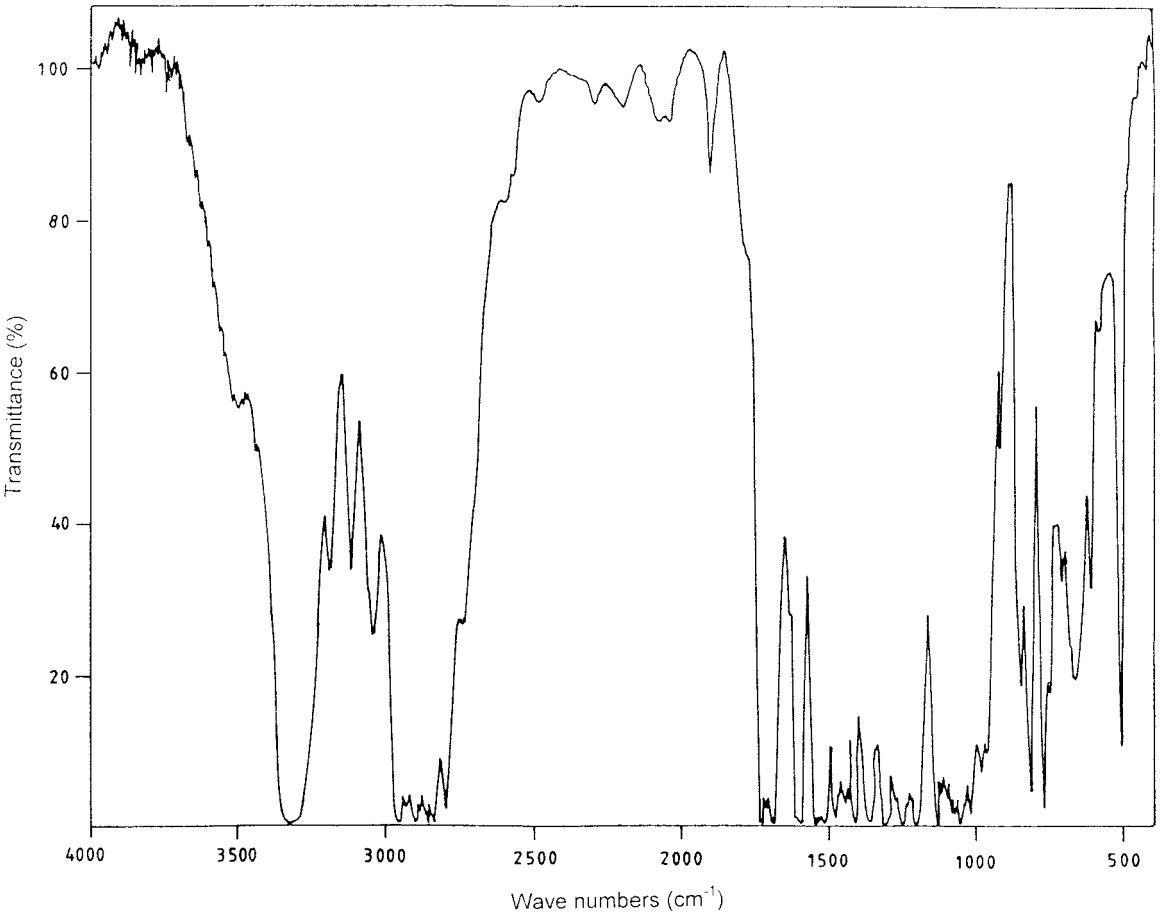

Figure 1 FTIR spectra of PU membranes.

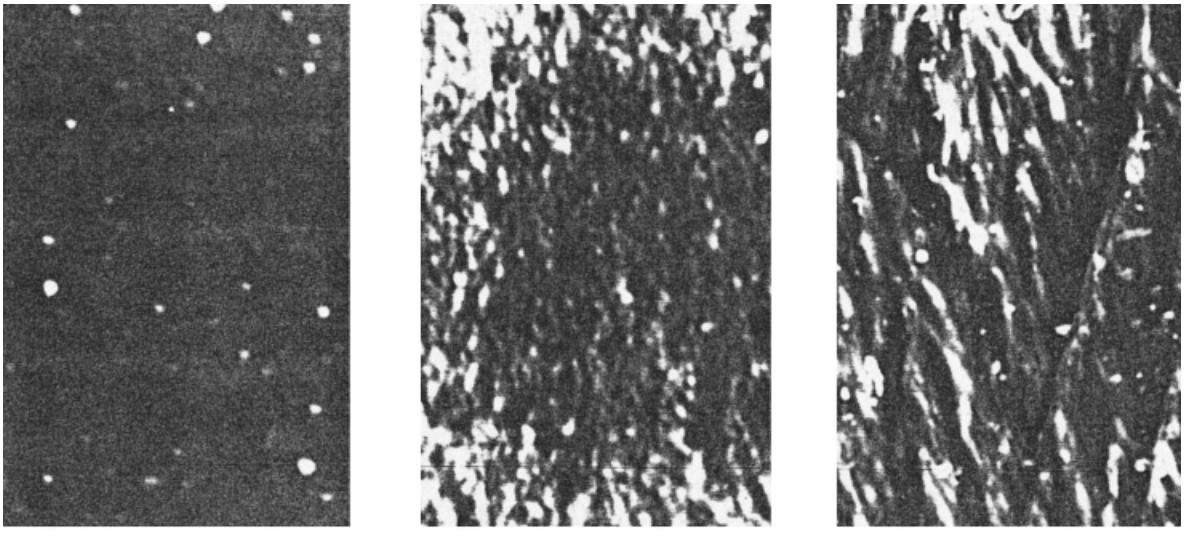

Figure 2 SEM micrographs of (a) PU, (b) $(AAm)_3$, and (c) $(IA)_3$ membranes.

Table III C'' Values (μg/mL) of the Membranes over Time

	t (h)									
Membrane	1	2	3	4	5	6	7	8	9	10
PU	1.4	2.0	2.5	3.2	3.8	4.1	4.8	5.1	5.9	6.3
$(AAm)_1$	3.8	4.3	4.9	5.6	6.1	6.9	7.0	8.2	8.8	9.4
$(AAm)_2$	3.0	3.2	4.0	4.5	5.3	6.2	7.0	7.5	8.0	9.2
$(AAm)_3$	4.8	6.7	8.4	10.3	11.4	13.2	14.8	15.1	17.0	18.9
$(IA)_1$	2.6	2.7	2.8	3.2	3.3	3.5	4.1	4.1	4.8	4.9
$(IA)_2$	2.5	2.6	2.6	3.0	3.2	3.8	4.1	4.8	5.1	5.2
$(IA)_3$	5.0	5.5	7.4	9.2	10.2	11.6	13.2	14.8	16.4	18.0

ness. By considering the total flux through the membrane and assuming small changes in C' during diffusion time, eq. 2 takes the form:

$$\frac{C''}{C'} = \frac{D \cdot A \cdot t}{V \cdot x} \tag{2}$$

where A is the area of the membrane (cm^2) and V is the volume of the half-cell (cm^3).[28–30]

Swelling Measurements

Swelling percentages ($S\%$) of the membranes were determined gravimetrically by swelling the membranes to a constant weigth in distilled water at 37°C. The $S\%$ values were calculated with the following equation:[31]

$$S\% = \frac{w - w_0}{w_0} \times 100 \tag{3}$$

FTIR and SEM Analyses of the Membranes

FTIR spectra of PU membranes were recorded with a Perkin-Elmer 1710 spectrophotometer. SEM analysis of 200 Å gold-coated membranes were performed with a JEOL (JSM 840A model) SEM.

RESULTS AND DISCUSSION

The wet thicknesses and the swelling percentages ($S\%$) of the membranes are presented in Table II. The highest thickness value was determined for the most swollen membrane $(AAm)_3$. As the hydrophilic character of the membranes was increased by adding AAm and IA monomers to the PU, the swelling percentage values were also increased.

The FTIR spectrum of the PU membrane presented in Figure 1. Because the specific groups of PU, AAm, and IA are same, similar absorption peaks were obtained for all membranes. From Figure 1, the PU membrane is characterized by the absorption peaks at 1070–1150 cm^{-1} (C—O-stretching), 1260–1410 cm^{-1} (O—H bending), 1560–1650 cm^{-1} (NH_2 bending), 1650–1710 cm^{-1} (C═O stretching), 1690–1740 cm^{-1} (urethane groups), 2880–2890 cm^{-1} (C—H stretching), 2850–2960 cm^{-1} (CH_3 groups), and 3300–3500 cm^{-1} (NH stretching in primary amide groups).[32]

Scanning electron micrographs of PU, $(AAm)_3$, and $(IA)_3$ membranes are presented in Figure 2. It was observed from the SEM results that the surface of PU membrane had a smooth and homogeneous appearance caused by nonporous structure (Fig. 2a). In contrast, PU membranes, $(AAm)_3$ and $(IA)_3$, have a porous structure (Figs. 2b and 2c).

Variations of C'' by t are listed in Table III. Because of the linear variation of C'' by t (assuming small changes in C' during diffusion time), it

Table IV D (cm^2/s), P (cm/s), and R Values of the membranes

Membrane	$D \times 10^9$	$P \times 10^7$	R
PU	1.03	1.95	0.997
$(AAm)_1$	1.62	2.26	0.996
$(AAm)_2$	2.09	2.51	0.995
$(AAm)_3$	7.06	5.43	0.996
$(IA)_1$	0.86	0.98	0.979
$(IA)_2$	1.39	1.21	0.977
$(IA)_3$	6.54	5.34	0.997

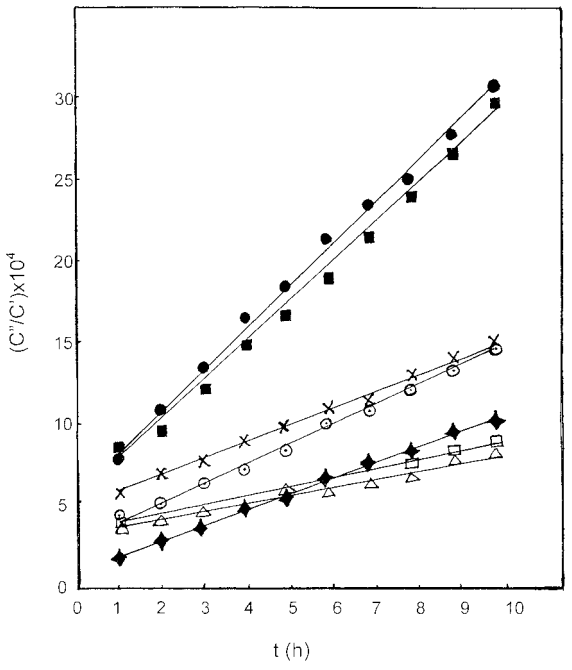

Figure 3 Increase in C''/C' of DCF-Na as a function of time at 37°C. Key: (♦) PU; (X) $(AAm)_1$; (○) $(AAm)_2$; (●) $(AAm)_3$; (△) $(IA)_1$; (□) $(IA)_2$; (■) $(IA)_3$.

can be thought that the diffusion rates (dC/dt) are constant for all membranes. It took much less time for all the membranes to reach therapeutic serum concentration range (0.7–1.5 μg/mL) than with the PU membrane.[33] At the end of 10 h, C'' values of $(AAm)_3$ and $(IA)_3$ membranes were three-times more than those of the PU membrane. This result can be explained by the hydrophlic character of the membranes. As the hydrophilicity of the membranes increases, the void volume between molecules also increases and the drug diffusion becomes easier.

Figure 3 shows the variation of C''/C' with time. Permeability coefficients, $P(D/x)$ of the membranes are calculated from the slopes of the lines by a curve-fit program with ~0.98–1.00 regression coefficient. The results are given in Table IV. As seen from this table, D and P values rapidly increase by adding hydrophilic monomer into PU. Comparision of Table II and Table IV shows that the permeabilities increase as swelling values of the membrane increase and the most permeable membrane is $(AAm)_3$.

CONCLUSION

The hydrophilic PU based membranes can be prepared by graft copolymerization of AAm and IA monomers with PU. These membranes are permeable for DCF-Na at 37°C. The therapeutic serum concentration range is reached for all membranes. As the hydrophilic character of the membrane increased, swelling percentage, D, and P values increased too. It can be concluded that $(AAm)_3$ and $(IA)_3$ membranes are suitable for development as a reservoir system.

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