Novel Polyurethane–Silicone Hydrogels

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SYNOPSIS

Polyurethane hydrogels derived from polysiloxane-based ultraviolet-curable polyurethane prepolymers and hydrophilic monomers were prepared and their properties were evaluated. The polyurethane prepolymers used in this study contained different arrangements of hard and soft segments and were derived from isophorone diisocyanate, neopentyl glycol, diethylene glycol, 1,4-butanediol, hydroxy-terminated polydimethylsiloxane, and 2-hydroxyethyl methacrylates. The hydrophilic monomers used were 2-hydroxyethyl methacrylate and N,N-dimethyl acrylamide. All compositions can be cured under ultraviolet (UV) and form hydrogels after hydration. The oxygen permeabilities of the hydrogels are much higher than those of nonsilicone hydrogels and decreased as the water contents increased. The tear strengths and moduli decreased as the water contents of the hydrogels increased. All hydrogels prepared showed good hydrolytic stability and did not absorb lysozyme. © 1995 John Wiley & Sons, Inc.

INTRODUCTION

Polyurethanes have broad applicability since their properties can be tailored by variations of their components: the diol chain extender, the flexible polyol, and the polyisocyanate.[1] Polyurethane is the most important polymer used in biomedical devices.[2]

Polyurethane hydrogels are claimed to have applications in the biomedical area. Blair and Hudgin disclosed the use of hydrophilic polyurethanes as soft contact lens material.[3] Gould and Johnston prepared interpenetrating networks of polyurethanes and by polymerizing diacrylates in the presence of hydrophilic polyurethanes.[4-7] These systems formed hydrogels and are claimed to have applications as contact lenses[5] and surgical implants.[8]

Ultraviolet-curable polyurethane prepolymers with well-defined hard–soft–hard segments, derived from diisocyanates, short-chain diols, and polypropylene glycols and end-capped with 2-hydroxyethyl methacrylate, were studied before,[9] and the hydrogels derived from such prepolymers were evaluated.[10,11] Polymers containing polysiloxane fragments have unique properties, such as low surface energy, low glass transition temperature, good thermal stability, and high gas permeability, which make them useful in many important applications.

Preparations of polysiloxane-based polyurethane prepolymers with different arrangements of hard segments in a manner similar to that of polypropylene-glycol-based prepolymers were described elsewhere.[12-14] In this study, polyurethane hydrogels derived from these polysiloxane-based polyurethane prepolymers are described.

EXPERIMENTAL

Materials and Monomers

The polyurethane prepolymers, their constituent monomers, and the hydroxy-terminated polydimethylsiloxane used in this study are described elsewhere.[13,14] N,N-dimethyl acrylamide (DMA, Aldrich Chemical) was used as received. 2-Hydroxyethyl methacrylate (HEMA) was redistilled in vacuo. Benzoin methyl ether (BME) was recrystallized from methanol.

Hydrogel Film Preparations

The polyurethane prepolymer and hydrophilic monomer were mixed in toluene with 0.2–0.5% BME added. The mix was introduced between two glass

plates (10 × 8 cm) and cured under a long wave ultraviolet (UV) lamp (from UVP) for 2 h. The film thickness was controlled by a Teflon gasket material which gave fairly consistent thickness of 0.25 mm. The films were extracted with toluene, dried, reextracted with boiling water, and then swollen to equilibrium in a phosphate-buffered saline (pH 7.30).

Characterization of Hydrogel Films

Mechanical testing was conducted in buffered saline on an Instron instrument, according to the modified ASTM D-1708 (tensile) and D-1938 (tear) procedures and were reported in g/mm^2 (1 MPa = 102 g/ mm^2), for tensile strength and modulus and g/mm (1 kN/m = 1020 g/mm), for tear strength.

Oxygen permeabilities were measured by the one chamber method with consideration of edge effect and probe configuration[15] and were reported in units of Barrer (Barrer = 10^{-11} cm^2 mL O$_2$/s mL mmHg).

The water contents were measured gravimetrically. The contact angles were measured by air-bubble method in buffered saline.

The hydrolytic stability was determined as follows: 12 preweighed dry films were saturated with buffered saline (pH = 7.4) and stored in sealed glass vials and then stored in an oven at 80°C. Three samples were removed after 3, 5, 7, and 14 days, respectively. They were washed with distilled water and dried at 80°C for 16 h. The percent weight losses of sample after different periods of testing were obtained by comparing the weight of dry sample before and after the testing.

The lysozyme uptake test was done by shaking hydrogel films of known weight (30–40 mg) in a vial containing a standard aqueous solution (5 g) with 500 ppm of lysozyme for a week. The amount of lysozyme remaining was measured by UV spectroscopy and the lysozyme uptake was reported as micrograms of lysozyme per milligram of hydrogel film, using poly(HEMA) hydrogels as controls.

RESULTS AND DISCUSSION

Polyurethane Prepolymers

The synthesis and characterization of UV-curable, polysiloxane-based polyurethane prepolymers and their precursors and intermediates have been described previously.[12-14] These prepolymers were prepared using isophorone diisocyanate (IPDI) as the diisocyanate; neopentyl glycol (NPG), diethylene glycol (DEG), and 1,4-butanediol (BD) as short-chain diols and hydroxy-terminated polydimethyl-siloxanes (PDMS) of molecular weight (M_n) 1500–

8000 as a flexible diol. These prepolymers were end-capped with HEMA and have three distinct types of hard segment. They are:
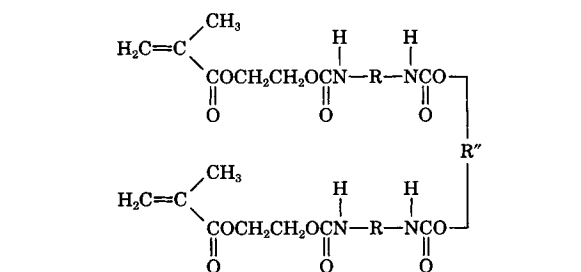
1. Prepolymers with well-defined hard–soft–hard segments as shown in **1**.
2. Prepolymers with soft–hard–soft segments as shown in **2**.
3. Prepolymers without a well-defined hard segment, where IPDI is used as the linkage between the polysiloxane and the end-capping HEMA. These prepolymers have the structure shown is **3**.
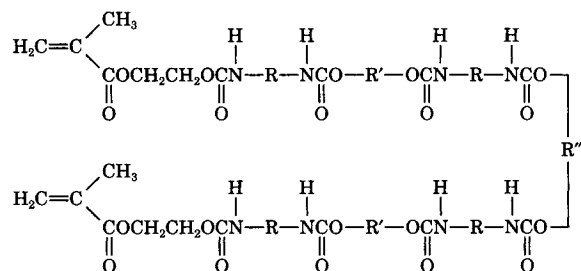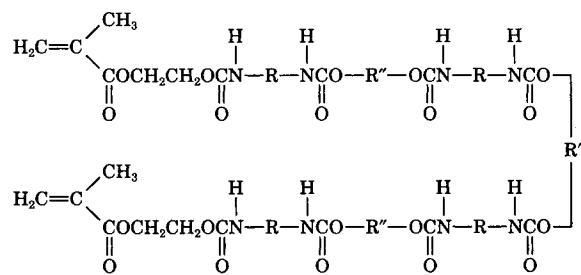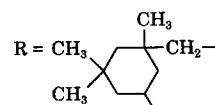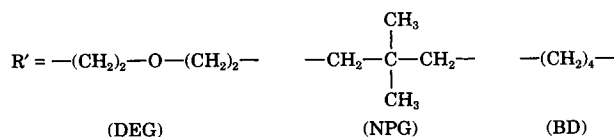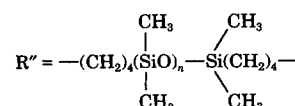
n	M_n of PDMS
16	1500
37	3000
57	4500
104	8000

For simplicity, abbreviations are used to designate the various prepolymers. IDS3H, IDS4.5H, IDS8H, INS3H, and INS4.5H represent prepolymers derived from IPDI, DEG (or NPG), and PDMS of molecular weight 3000, 4500, and 8000 and end-capped with HEMA and having the structure **1**. IDS4.5HA has the same structure, but has $\frac{1}{4}$ of HEMA end-capping replaced with allyl alcohol. IS1.5NH represents a prepolymer with soft–hard–soft segment, using PDMS of molecular weight 1500 as the soft segment and has the structure **2**. IS3H represents a prepolymer without well-defined hard segment and has the structure **3**.
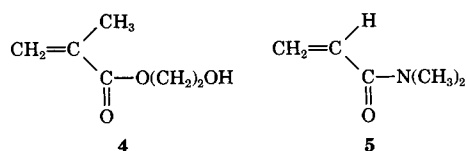
Prepolymers used in this study are tabulated in Table I with the mechanical properties of the cured prepolymers summarized in Table II. These prepolymers have tensile moduli ranging from 110 to 5200 g/mm² and tear strengths ranging from 9 to 64 g/mm. In addition, all cured prepolymers have high oxygen permeabilities (250 Barrer or higher) due to a high siloxane content. These features make the prepolymers useful as a base for making hydrogels with a broad range of properties, including high oxygen permeability.

Hydrogel Syntheses

Hydrogels are normally prepared by curing a monomer mix containing at least one hydrophilic mono-

mer, one crosslinker, a diluent, and an initiator. Curing can be initiated by UV or thermal initiators. The cured polymers are then hydrated to form hydrogels. In the preparation of silicone hydrogels, a siloxane-containing monomer prepolymer or macromer is included in the monomer mix monomer mix.

In order to optimize the water content and properties, hydrophilic monomers with different water affinity were employed. The hydrophilic monomers used were 2-hydroxyethyl methacrylate, (HEMA, **4**) and N,N-dimethyl acrylamide, (DMA. **5**).

$$CH_2=C\begin{array}{l}{}^{\diagup CH_3}\\{}_{\diagdown C-O(CH_2)_2OH}\\{}\quad\|\\{}\quad O\end{array} \qquad CH_2=C\begin{array}{l}{}^{\diagup H}\\{}_{\diagdown C-N(CH_3)_2}\\{}\quad\|\\{}\quad O\end{array}$$

$$\textbf{4} \qquad\qquad\qquad \textbf{5}$$

Thus, the monomer mixes were prepared by mixing the prepolymer and the hydrophilic monomer with BME as the initiator and toluene as the diluent. Hydrogel films were prepared by curing the monomer mixes under UV, followed by an appropriate solvent treatment to remove extractables, and hydration in boiling water. The hydrogel films were then saturated in a buffered saline before characterization.

Hydrogel Properties

In the following, key composition–property relationships are described for the hydrogels derived from the prepolymers described in Table I and DMA.

Water Content and Oxygen Permeability

Figure 1 shows the effect of DMA concentration in the monomer mix on the water content and oxygen

Table I   Polyurethane Prepolymers Used in this Study

Prepolymer Name	Class[a]	Composition Soft Segment/Hard Segment/End Cap			
IDS3H	h-s-h	Si-3000 (1)	DEG (2)	IPDI (4)	HEMA (2)
IDS3.6H	h-s-h	Si-3600 (1)	DEG (2)	IPDI (4)	HEMA (2)
IDS4.5H	h-s-h	Si-4500 (1)	DEG (2)	IPDI (4)	HEMA (2)
IDS4.5HA	h-s-h	Si-4500 (1)	DEG (2)	IPDI (4)	HEMA(1.5) ALLYL (.5)
INS3H	h-s-h	Si-3000 (1)	NPG (2)	IPDI (4)	HEMA (2)
INS4.5H	h-s-h	Si-4500 (1)	NPG (2)	IPDI (4)	HEMA (2)
IS1.5NH	s-h-s	Si-1500 (2)	NPG (1)	IPDI (4)	HEMA (2)
IBS3H	h-s-h	Si-3000 (1)	BD (2)	IPDI (4)	HEMA (2)
IBS4.5H	h-s-h	Si-4500 (1)	BD (2)	IPDI (4)	HEMA (2)
IS3H	s	Si-3000 (1)		IPDI (2)	HEMA (2)

[a] h-s-h and s-h-s represent hard-soft-hard and soft-hard-soft block structure, respectively; s represents prepolymer without well-defined hard segment.

**Table II   Mechanical Properties of Cured Polyurethane Prepolymers and
Hydrogels Derived from These Prepolymers and DMA at 70 : 30 Weight Ratio**

Prepolymer	Tensile Modulus (g/mm²)		Tear Strength (g/mm)	
	Prepolymer	Hydrogel	Prepolymer	Hydrogel
INS3H	4800	350	64	9
INS4.5H	1400	250	23	6
IS1NH	5200	700	71	9
IS3H	620	250	9	3
IDS3H	2900	220	37	9
IDS3.6H	2000		28	
IDS4.5H	1100	180	17	3
IDS4.5HA	460	150	9	3
IBS3H	1240	530	28	13
IBS4.5H	575	190	11	5

permeability of polyurethane–silicone hydrogels derived from the prepolymer INS3H and DMA. Figure 2, shows the relationship between oxygen permeability and water content for hydrogels derived from the same compositions. As expected, the higher the amount of hydrophilic monomer (DMA) used, the higher the water content of hydrogels derived. Oxygen permeability decreased initially from 280 Barrers as the concentration of DMA increased, hiting a minimum of 40 Barrers when 60 parts of DMA was used (60% water in the hydrogel). This observation also indicates that oxygen permeability initially decreases as the silicon content in the hydrogels decreases. But once the water content reaches a certain level, the hydrogels behaves more like a traditional nonsilicone hydrogels. When another

prepolymer IDS3H was used, the same oxygen permeability–water content relationship was observed (see Fig. 3). The curves in Figures 2 and 3 are superimposable at any water content within error of the measurements. This indicates that the oxygen permeability of silicone hydrogels comes from the same mechanism—the siloxane and water content. The percent siloxane content of these two prepolymers are the same. This translates into the same percent of siloxane in the hydrogels derived from these prepolymers since the composition of same hydrophilic monomer was used.

To further illustrate the importance of siloxane groups on oxygen permeability of silicone-based polymers, Figure 4 shows the relationship of silicon atom content in polysiloxane-based elastomer and
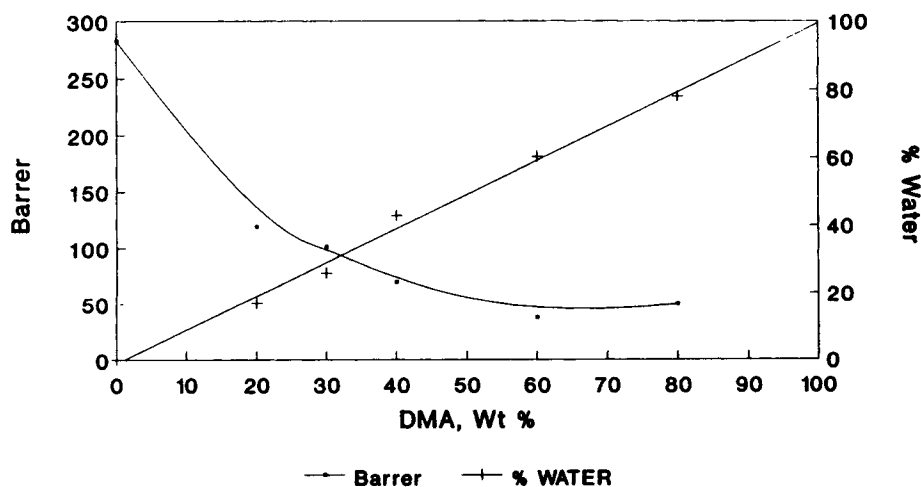
Figure 1   Relationship between water content–oxygen permeability and DMA concentration in polyurethane–silicone hydrogels derived from INS3H and DMA.
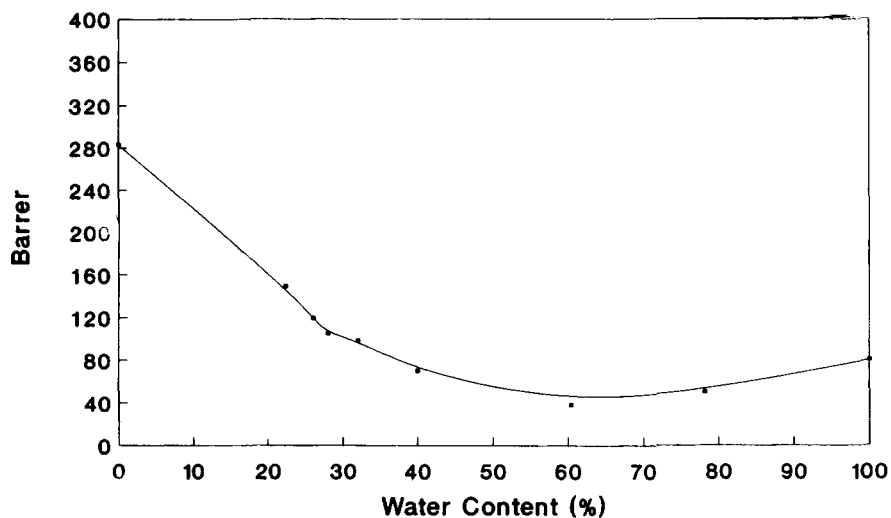
Figure 2   Relationship between oxygen permeability and water content for hydrogels derived from 1NS3H and DMA.

hydrogels using the polyurethane–silicone prepolymer IDS3H and DMA as an example. This relationship is a "mirror image" of the relationship between oxygen permeability and water content for the comparable compositions (as shown in Fig. 3). The oxygen permeability bottoms out at a silicon atom content of around 4% and a Barrer value of 40, which corresponds to a hydrogel with a water content of around 60%.

Regardless of the decrease in oxygen permeability with increasing water contents, these silicone hydrogels have oxygen permeabilities far higher than

those of traditional hydrogels.[16] For example, hydrogels based on poly(2-hydroxyethyl methacrylate), have an oxygen permeability of 8 Barrers. The silicone hydrogels discussed in this study, with the same water content (38%), have an oxygen permeability of 90–100 Barrers.

Comparison with Hydrogels Derived from PPG-Based Polyurethane Prepolymer

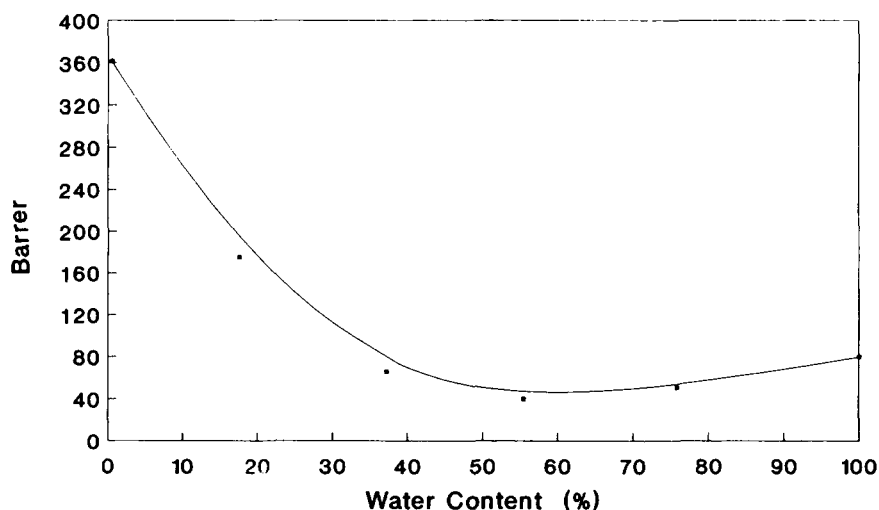Polypropylene glycol (PPG) of M_n 4000 gave a polyurethane prepolymer of the same structure as

Figure 3   Relationship between oxygen permeability and water content for hydrogels derived from IDS3H and DMA.
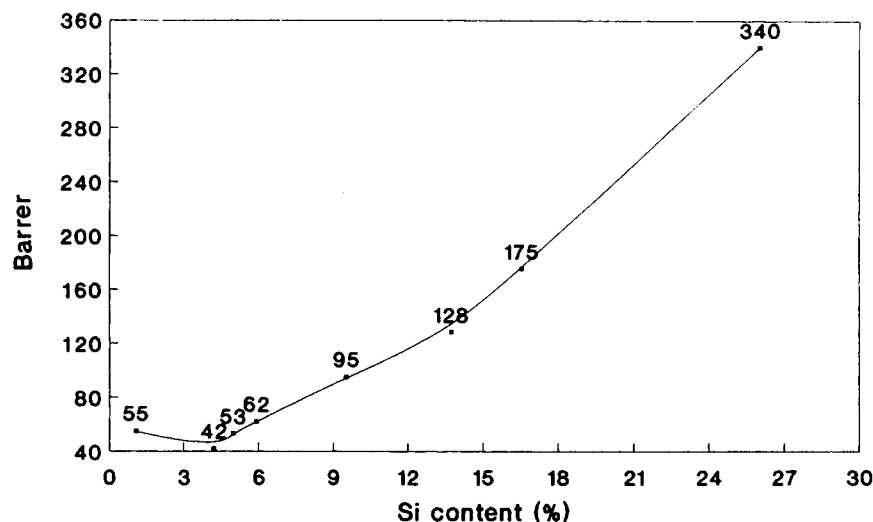
Figure 4 Relationship between oxygen permeability and silicon atom content in polyurethane–siloxane-based elastomer and hydrogels derived from prepolymer IDS3H and DMA.

INS3H. It had an oxygen permeability of 36 Barrers. The relationship between oxygen permeability and water content for this class of polyurethane hydrogels is similar to that for hydrogels based on polysiloxane except that the lowest oxygen permeability of hydrogels derived occurred at a different water content (around 30%) and with different Barrer values (25 Barrers).[10] Figure 5 shows a comparison of oxygen permeability–water content relationships for both kinds of hydrogels as well as that for traditional

hydrogels based on hydrophilic monomers only.[16] Both classes of nontraditional hydrogels have oxygen permeability higher than that of traditional hydrogels. However, when the water content is higher than 60%, the oxygen permeabilities of all classes of hydrogels are about equal. This means the contribution of hydrophobic flexible groups, such as PPG and siloxane, diminishes as water content increases in a hydrogel, while the contribution of water to oxygen transport in the hydrogel becomes pre-
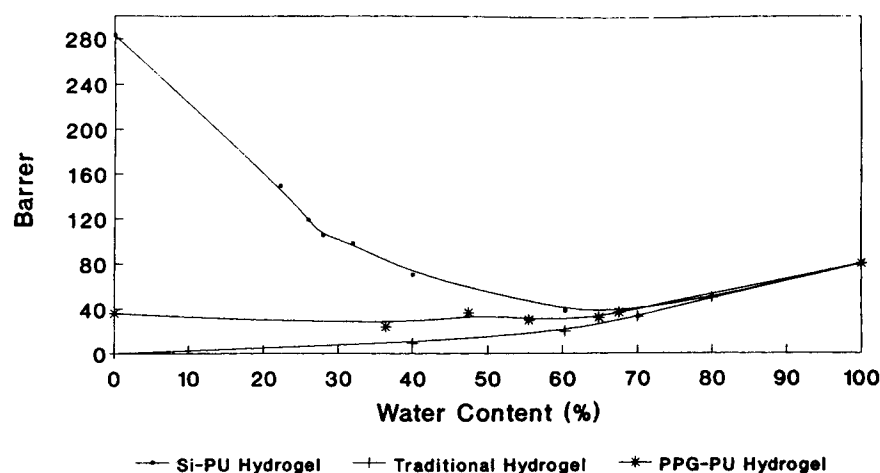

Figure 5 Relationship between oxygen permeability and water content for hydrogels derived from PPG- and PDMS-based polyurethane prepolymers, as well as traditional hydrogels based on hydrophilic monomer.
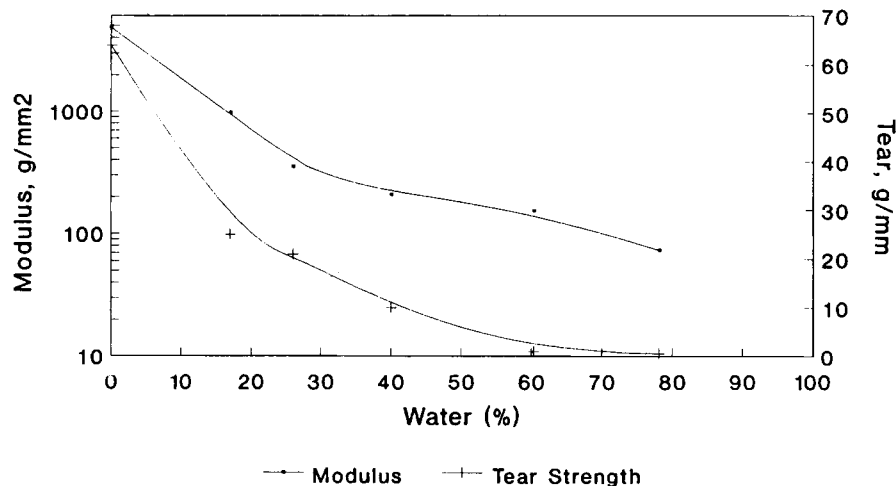
Figure 6 Relationships between modulus–tear strength and water content in the hydrogels derived from a polyurethane prepolymer INS3H and DMA.

dominant when the water content is higher than 60%. These results suggest that it is not worthwhile to prepare a silicone hydrogel with a water content higher than 60% if high oxygen permeability is desired for a particular application.

Mechanical Properties

Table II also lists the mechanical properties of hydrogels derived from the prepolymers listed in Table I and DMA at the weight ratio of 70:30. Because of the same amount of DMA used, these hydrogels have the same water content (24–26%). The tensile mod-

ulus and tear strength data suggested that the mechanical properties of these polyurethane–silicone hydrogels correlate well with those of their parent prepolymers when the latter are cured. Hydrogels derived from polyurethane prepolymers with well-defined hard segments showed higher modulus and better tear strength compared to those derived from polyurethane prepolymers without well-defined hard segments. The difference in mechanical properties in hydrogels are narrower compared to those of the cured prepolymers due to dilution effects with DMA and the increased water content in the hydrogels.

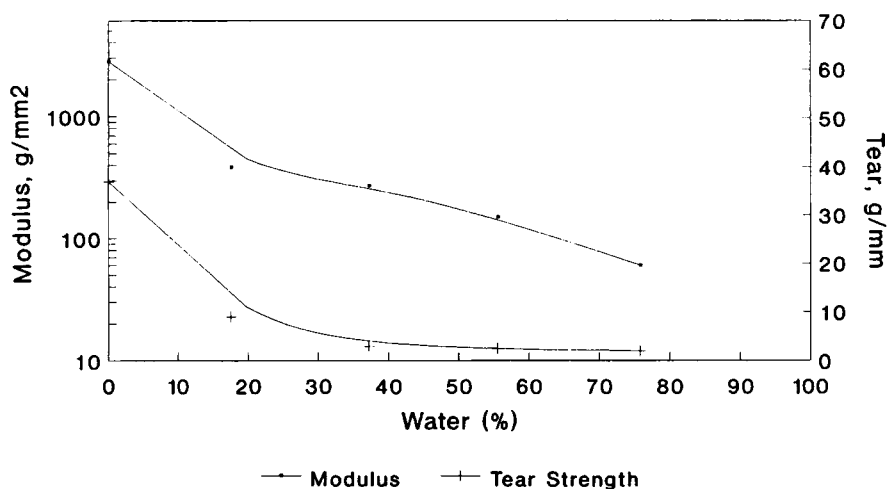Figure 6 shows the relationship between modulus,

Figure 7 Relationships between modulus–tear strength and water content in the hydrogels derived from a polyurethane prepolymer IDS3H and DMA.

Table III   Hydrolytic Stability Testing Results of Selected Hydrogels Derived from Selected Prepolymers

Prepolymer	Water (%)	3 Days	Percent Weight Loss/Percent Water		
			5 Days	7 Days	14 Days
INS3H	25.4	0.59/24.5	0.56/25.4	0.77/23.8	0.89/23.9
IDS3H	38.9	1.27/38.4	0.83/38.7	2.0/38.4	2.10/38.9
IDS4.5H	38.8	0.08/39.7	0.82/41.4	0.23/37.6	1.44/41.4
IS1NH	22.3	0.24/23.3	1.15/26.7	0.34/23.4	1/13/23.4
IBS4H	38.2	1.09/39.6	0.86/41.5	0.45/41.6	1.90/40.1

tear strength, and water content in hydrogels derived from the polyurethane prepolymer INS3H and DMA. As expected, the moduli and tear strengths of the hydrogel films decreased dramatically as the hydrophilic monomer (or water) content increased or the amount of INS3H decreased. Figure 7 shows the same relationship for hydrogels derived from IDS3H and DMA. For the hydrogels derived from other polyurethane prepolymers shown in Table I, and DMA, the moduli and tear strengths are related to water content in the same fashion.

Hydrolytic Stability

Hydrolytic stability is an important property in determining the suitability of a hydrogel for use as

medical devices such as a contact lens. Hydrolytic stability is a measure of susceptibility to degradation during thermal disinfection and shelf life. In our hydrolytic stability study, the tests were carried out at 80°C, in buffered saline for a total of up to 14 days. The stability was demonstrated by the weight loss of the dry sample as well as the change in water content for the hydrogel. Weight loss of 5% or lower over a 14-day period was considered stable.

Table III lists the stability data for selected hydrogels derived from different prepolymers and DMA at different weight ratios. In any case, the weight loss was 2.1% or lower after 14 days of testing at 80°C. In addition, within experimental error, there was no change in water content. This suggested that this class of polyurethane–silicone hydrogels is

Table IV   Lysozyme Uptake of Polyurethane–Silicone Hydrogels as Well as Some Known Hydrogels Used as Contact Lenses

Composition (Feed)	Trade Name (Product)	Water (%)	Lysozyme Uptake (μg/mg)
Poly(HEMA)	Soflens	38	0–1
Poly(HEMA-co-MAA)[a] 98/2	Vistamac	58	25
Poly(HEMA-co-MMA-co-NVP)[b]	B&L 70	70	4
Polyurethanes			
INS3H/DMA			
70/30		26	0.0
60/40		40	0.5
IDS3H/DMA			
70/30		25	0.5
60/40		40	0.5
IDS4.5H/DMA			
60/40		37	2.0

[a] MAA, methacrylic acid.
[b] MMA, methyl methacrylate; NVP, N-vinyl pyrrolidone.

Table V   Properties of Polyurethane–Silicone Hydrogels Derived from INS3H and HEMA

Composition	Percent Water	Barrer[a]	Modulus	Hydrolytic Tests[b]
INS3H : HEMA				
70 : 30	8.9	189	3240	0.05/0.07/0.0/0.0
60/40	13.1	112	1830	0.9/1.3/1.2/1.6

[a] Oxygen permeability.
[b] Weight loss after 3, 5, 7, and 14 days at 80°C.

hydrolytically stable, which was contrary to what had been found for similar hydrogels derived from PPG-based polyurethane prepolymers.[11]

Protein Absorption

One of the critical factors for a polymeric material to be considered for biomedical applications is its interaction with the bio-substrate. For example, polyurethane materials useful as implants should not absorb protein from the blood, otherwise thrombosis can occur. Similarly, for hydrogel materials to be considered for ophthalmic applications, they should not absorb significant amounts of protein from the tear fluid. Protein absorption on the lens surface can adversely affect the performance of a contact lens and could ultimately lead to ocular disease.

Hydrogels based on P(HEMA), a class of hydrogels used most often in contact lenses, do not pick up any significant amount of lysozyme. Table IV illustrates some lysozyme uptake data of polyurethane–silicone hydrogels as well as those of some established soft contact lens products for comparison.

Regardless the water content, all the polyurethane–silicone hydrogels prepared in this study had insignificant lysozyme uptake and were essentially equivalent to P(HEMA) hydrogels. Earlier results on hydrogels based on PPG-based polyurethane prepolymers also showed little protein uptake.[10] Hydrogels based on a copolymer of 2-hydroxyethyl methacrylate and methacrylic acid, poly(HEMA-co-MAA), which is used as a disposable contact lens, have a very high level of lysozyme uptake.

In addition to polyurethane–silicone hydrogels derived from polyurethane prepolymers with DMA, hydrogels derived from a prepolymer INS3H and HEMA were also prepared, with properties tabulated in Table V. Because HEMA gives less water content to a hydrogel compared to DMA, these hydrogels had lower water content and a higher modulus for the same amount of hydrophilic monomers used.

They are all hydrolytically stable. However, the hydrogel films are hazy when higher levels of HEMA (40% and higher) are used. Because of inferior optical quality, stiffness, and low water content, they are not useful as hydrogel lens materials. In summary, polysiloxane-based polyurethane prepolymers exhibit a broad range of mechanical properties and have excellent oxygen permeability. The properties of the hydrogels derived from theses prepolymers can be tailored easily to suit a particular application. They have oxygen permeabilities higher than those of nonsilicone hydrogels of any known class.

CONCLUSION

UV-curable polyurethane–siloxane prepolymers can be used to prepare hydrogels with hydrophilic monomers. These hydrogels have a broad range of modulus, excellent tear strength, and higher oxygen permeability than conventional hydrogels. In addition, they are hydrolytically stable and do not pick up significant amounts of lysozymes.

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