Control of Properties in Silicone Hydrogels by Using a Pair of Hydrophilic Monomers

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SYNOPSIS

Silicone hydrogels have been under intensive investigation for use in the biomedical field, especially as contact lenses. When silicone hydrogels were prepared using a combination of N-vinyl pyrrolidone and N,N-dimethyl acrylamide as the hydrophilic monomers, it was found that the surface wettability of these hydrogels can be improved with the mechanical properties and that water contents are in the acceptable range for certain applications, such as contact lenses. © 1996 John Wiley & Sons, Inc.

INTRODUCTION

Hydrogels are water-containing polymer networks. In water, these polymers swell to an equilibrium volume and maintain their shape. Hydrogels have been used in a variety of applications, particularly as contact lenses.¹ These contact lenses are derived almost exclusively from 2-hydroxyethyl methacrylate, glycerol methacrylate, N-vinyl pyrrolidone (NVP, 1), and acrylamides, such as diacetonacrylamide or N,N-dimethylacrylamide (DMA, 2).¹



Hydrogels which are currently used as contact lenses have equivalent water contents ranging from 38 to 75%. The oxygen permeability of these hydrogel materials, which depends exclusively on water content, falls in the range of 8 to 40 in Barrer units (1 Barrer = 1 Dk = 1×10^{-11} cm² mL O₂/s mL mmHg). The tensile moduli of these hydrogels are in the range of 20 to 140 g/mm^2 , and tear strengths

Existing hydrogel lenses are suitable for daily wear. However, because of insufficient oxygen transport, they cause excessive corneal swelling in overnight wear due to hypoxia.² Attempts to increase oxygen transport, either by using materials with higher water content or by employing a thinner lens, generated only limited success due to other complications.¹ Hydrogels based on polysiloxanes, or so gels based on polysiloxanes (silicone hydrogels), have been under active investigation since the early $1970s^1$ to develop viable compositions by taking advantage of the high oxygen permeability of polysiloxanes.³

For hydrogels to be useful for contact lens applications, in addition to oxygen permeability, water content, and mechanical properties, they must maintain excellent surface wettability. Although silicone hydrogels can be made with appropriate mechanical properties and excellent oxygen permeability, it is difficult to maintain good wettability in the ocular environment due to the inherent hydrophobic character of silicone-based materials.

This paper discusses approaches to manipulating water content, surface wettability, and mechanical properties in silicone hydrogels based on polysiloxane-based prepolymers and methacryloxypropyl tris(trimethylsiloxy)silane, (TRIS, **3**),

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are in the range of 1 to 5 g/mm. The water content, modulus, and tear strength of hydrogels depend on the nature of monomers and crosslinking density.¹



using a pair of hydrophilic monomers, NVP and DMA.

EXPERIMENTAL

Monomers and Prepolymers

The preparation of a polyurethane prepolymer IDS3H, 4 (which is based on isophorone diisocyanate, diethylene glycol, poly (α , ω) hydroxybutyl-terminated polydimethylsiloxane of molecular weight 3000, and 2-hydroxyethyl methacrylate), was described elsewhere.⁴ A methacrylate-capped polydimethylsiloxane prepolymer, M_2D_{25} (structure shown as 5), and methacryloxyethyl vinyl carbonate (HE-MAVC) were also described elsewhere.^{5,6} TRIS (over 98.5% purity, containing less than 0.02% dimer) was obtained from Silar, Inc. (Scotia, New York) and used as received. DMA and NVP were distilled under reduced pressure. n-Hexanol and 2-hydroxy-2,2-dimethyl acetophenone (known as Darocur-1173; EM Industries, Hawthorne, New York), were used as received.

Hydrogel Synthesis

A polydimethylsiloxane-based polyurethane prepolymer IDS3H or methacrylate-capped prepolymer

 Table I
 Polyurethane–Polysiloxane-based

 Silicone Hydrogel Lens Materials

Hydrogel Lens	1	2	
Chemical Composition			
IDS3H/TRIS/DMA	30/30/40	35/35/30	
Water Content, %	38	24	
Modulus	60	80	
Clinical Performance			
(4–6 hours)			
Wettability	2.2	2.0	
Lipid Deposits	1.5	1.7	

 M_2D_{25} , TRIS, and a hydrophilic monomer, in chosen weights to a total of 100 parts, were mixed with 40 parts of *n*-hexanol and 0.2 part of Darocur-1173. The monomer mix was placed between two glass plates (10 cm \times 8 cm) and cured under a long-wave UV lamp (UVP Inc., San Gabriel, California) for 2 h. Film thickness was controlled by a Teflon gasket which gave fairly consistent thicknesses of 0.25 mm. The films were extracted with ethanol for 16 h, dried in a vacuum oven at 70°C for 16 h, boiled with distilled water for 4 h, and swollen to equilibrium in phosphate-buffered saline (pH 7.30) before characterization.

Characterization of Hydrogel Films

The water content and the amounts of extractables in ethanol were measured gravimetrically. Mechanical testing was conducted in phosphate-buffered saline on an Instron instrument according to modified ASTM D-1708 (tensile) and D-1938



Figure 1 The relationship between modulus, tear strength, and water content in silicone hydrogels based on IDS3H/TRIS/DMA.

Formulation	1	2	
Chemical Composition IDS3H/TRIS/NVP/HEMAVC	30/30/40/0.1	35/35/30/0.1	
Properties Water Content %	37	25	
Modulus Surface Wettability	430 Good	570 Good	

 Table II
 Polyurethane–Polysiloxane-based Silicone Hydrogel with NVA

 as the Hydrophilic Monomer

(tear) procedures, and were reported in g/mm² (1 MPa = 102 g/mm²) for tensile strength and modulus, and g/mm (1 kN/m = 1020 g/mm) for tear strength. The oxygen permeabilities were measured by the one-chamber method⁷ with consideration of edge effects and probe configuration, and were reported in units of Barrer (1 Barrer = 10^{-11} cm² mL O₂/s mL mmHg).

Contact Lens Fabrication by Cast Molding

Selected monomer mixes containing prepolymer, TRIS, and a choice of hydrophilic monomers in *n*-hexanol were cast-molded under UV into lenses, against molds fabricated from a copolymer of acrylonitrile (Barex-210; BP Chemical, Cleveland, Ohio) and polypropylene.⁸ The released lenses were extracted with ethanol for 48 h, boiled in distilled water for 4 h, and thermally disinfected in a phosphate-buffered saline prior to on-eye evaluation.

Clinical Evaluations of Hydrogel Lenses

The fully processed hydrogel lenses were clinically evaluated only after approval for testing was granted. The steps toward its approval were strictly followed according to the FDA regulations regarding new contact lens materials. Clinical evaluation of hydrogel lenses was conducted using at least seven subjects, according to a standard protocol used within Bausch & Lomb. The lenses were analyzed after a minimum of 4 h for wettability and surface deposition. The surface wettability rating scale was 0-4, with 0 representing two-thirds of the anterior surface nonwettable by the tear film and 4 representing complete wetting. The deposition scale was also 0-4, with 0 representing no surface deposit and 4 representing multiple deposits of 0.5-mm diameter or larger.

RESULTS AND DISCUSSION

Silicone Hydrogels Derived from Polysiloxanebased Prepolymers, TRIS, and DMA

Because of favorable curing rates, methacrylatebased polysiloxane prepolymers have been studied extensively in targeting silicone hydrogels for contact lens applications.¹ This study employed two classes of polysiloxane-based prepolymers endcapped with methacrylate groups:

 Table III
 Polyurethane-Polysiloxane-based Hydrogels: Formulations and Hydrogel Properties

NVP/DMA	40/0	38/2	35/5	30/10	20/20	0/40
% Water	37	45	44	41	41	38
O2	96	95	115	96	87	96
Modulus	430	280	150	80	79	63

IDS3H = TRIS = 30 parts; NVP + DMA = 40 parts.



Figure 2 The relationship between modulus, water content, and amounts of DMA in silicone hydrogels based on IDS3H/TRIS/NVP/DMA with IDS3H = TRIS = 30 parts and DMA + NVP = 40 parts.



Both prepolymers have been used in formulations with DMA and TRIS to give hydrogels with mechanical properties in the range useful for biomedical applications including contact lenses.⁹⁻¹¹ TRIS is included to maintain high oxygen permeability as well as to lower the modulus and improve tear strength. DMA was chosen for its hydrophilicity and gives a much higher water content to a hydrogel than alcohol-containing monomers. Also, it copolymerizes well with methacrylates.

Figure 1 gives the relationship of both modulus and tear strength to water content for hydrogels based on IDS3H/TRIS/DMA, with IDS3H and TRIS used in equal amounts. These hydrogels have excellent mechanical properties when water contents are in the range of 20-60%. Because it is desirable for oxygen permeability of silicone hydrogels to be as high as possible, we focused on hydrogels with water contents below 50%.

Clinical Performance of Silicone Hydrogel Lenses with DMA as the Only Hydrophilic Monomer

Because of the hydrophobicity and the tendency of siloxane fragments to migrate to a low-energy air interface, it is difficult to maintain the surface wettability of silicone hydrogels. However, it was found that the surface wettability of silicone hydrogel can be markedly improved if the siloxanebased hydrogel formulations are cast against polar, plastic plaques or molds fabricated from Barex-210 (a copolymer of acrylonitrile and butyl acry-



Figure 3 The relationship between modulus, water content, and amounts of DMA in silicone hydrogels based on IDS3H/TRIS/NVP/DMA with IDS3H = TRIS = 34 parts and DMA + NVP = 32 parts.

late).¹² Plastic molds fabricated from Barex-210 were used to create the anterior surface of silicone hydrogel lenses derived from IDS3H, TRIS, and DMA.

Table I lists properties of two formulations for silicone hydrogels with water contents of 24 and 38%, respectively. When they were used to prepare lenses and clinically tested, they showed good initial wettability. However, after 4–6 h of wear, the surface wettability decreased to an unacceptable range (below 3.0), with a 2.0 rating on a scale of 4.0. Simultaneously, lipidlike deposits built up to an unacceptable level (1.5). Regardless of the difference in water content, these two silicone hydrogel lenses exhibited equally poor clinical performance in surface wettability and deposits.

Silicone Hydrogels with NVP as the Only Hydrophilic Monomer

NVP has been used frequently to prepare hydrogel contact lenses of water content over 40% because of its excellent hydrophilicity.¹ In those hydrogel lenses containing NVP, it was found that the lens surface is very lubricious, indicating excellent surface wettability. It is interesting to note that NVP is always used in combination with methacrylate monomèrs in making hydrogel lenses,¹ even though it does not copolymerize well with acrylic monomers.¹³ However, with the help of a novel crosslinker, HEMAVC, **6**), which has both vinyl carbonate and methacrylate groups,



Figure 4 The relationship between modulus and the ratio of NVP/DMA in silicone hydrogels based on IDS3H/TRIS/NVP/DMA with water contents of 24–38%.

NVP/DMA	40/0	30/10	20/20	0/40	
% Water	28	28	32	29	
O2	114	113	101	97	
Modulus	369	146	106	90	

Table IVM2D25/TRIS-based Hydrogels:Formulations and Hydrogel Properties

 M_2D_{25} = 13 parts, TRIS = 47 parts and NVP + DMA = 40 parts.



NVP can photocopolymerize efficiently with a crylic monomers. 6,14

NVP was used to replace DMA in the formulations listed in Table I as well as in other siloxanebased formulations. Table II lists the initial formulation studies for polyurethane-polysiloxane hydrogels using the same formulations as those listed in Table I, except NVP replaced DMA and HE-MAVC was the extra crosslinker (0.3% of NVP weight; 0.1% of total). The NVP-based hydrogels had the same water content as those of DMA-based hydrogels. However, a comparison of moduli showed that NVP produces hydrogels which are 6 times stiffer than DMA analogs.

It should be noted here that, because of the similarity in molecular weight of NVP and DMA (NVP

Formulation NVP/DMA	IDS3H	-based	M_2D_{25} -based	
	30/10	0/40	30/10	0/40
Wettability	3.3	2.3	3.9	3.5
Deposits	0.2	1.4	1.0	1.6

= 111; DMA = 99), Formulation 1 in Table I and Formulation 3 in Table II contained similar levels of crosslinkers (IDS3H and HEMAVC) on weight and molar bases. The mol % of crosslinkers was 1.45% and 1.71% of monomers (TRIS, DMA, and NVP combined), respectively, for Formulation 1 (DMA-based) and Formulation 3 (for NVP-based). So, although the minor difference in crosslinking density could contribute some change in modulus associated with NVP formulation, it could not be held responsible for the modulus which was 6 times that of DMA-based formulation.

Because of the high modulus, NVP-based formulations are not suitable for use as contact lenses.

Combination of DMA and NVP as the Hydrophilic Monomers in Silicone Hydrogels

One of the objectives of this study was to obtain wettable silicone hydrogels with acceptable mechanical properties. With DMA, low modulus was achieved along with poor surface wettability. With NVP, good surface wettability was achieved but with too-high moduli. Since both hydrophilic monomers give hydrogels with the same water content, com-



Figure 5 The relationship between modulus, water content, and amounts of DMA in silicone hydrogels based on M2D25/TRIS/NVP/DMA with $M_2D_{25} = 17$ parts, TRIS = 47 parts, and DMA + NVP = 40 parts.

bining these two monomers in a series of formulations may produce silicone hydrogels with good wettability as well as low modulus.

The formulation studies were conducted using a prepolymer (either IDS3H or M2D25) and TRIS at levels equal to the siloxane-containing monomer, and NVP/DMA at varying ratios. Some formulations were used to cast lenses.

Water Content, Oxygen Permeability, and Mechanical Properties of Silicone Hydrogels With Varying Ratios of NVP/DMA

Table III lists formulations derived from IDS3H/ TRIS at 30 parts each and varying amounts of NVP/ DMA (total 40 parts), along with key properties of hydrogel films prepared from them. As expected, water content (at around 38%) and oxygen permeability (above 90 Dk) of these hydrogels showed little variation with the ratios of NVP/DMA. However, tensile modulus changed dramatically with the weight ratio of NVP/DMA. The relationship of water content and tensile modulus to the amount of DMA is also shown in Figure 2. By gradually replacing NVP with DMA, the modulus dropped dramatically to about one-third of NVP value when only 5 parts of NVP was replaced, and reached an asymptotic level $(60-80 \text{ g/mm}^2)$ when only 10 parts (out of 40) of NVP was replaced. This nonlinear change in modulus was advantageous for developing a silicone hydrogel with high levels of NVP to maintain certain properties inherent to its copolymers while obtaining the desired low modulus.

In addition to the formulations shown in Table III, polyurethane-polysiloxane hydrogels based on the same components but having water contents as low as 25% were also studied. In those formulations, equal amounts of IDS3H and TRIS were used with varying relative amounts of NVP and DMA. Figure 3 gives the relationship between water content, modulus, and the amount of DMA in the combined DMA/NVP hydrophilic monomers at 32 parts, for formulations based on IDS3H/TRIS/DMA/NVP with IDS3H = TRIS = 34 parts. Again, it was found that the water content stayed very flat at 25-30% with respect to the change in the ratio of NVP to DNA. The modulus dropped dramatically from 610 to 80 g/mm² when the amount of DMA used was changed from 0 (with 32 parts of NVP) to 32 (no NVP). Figure 4 shows the effect of NVP/DMA ratio on the modulus of polyurethane-polysiloxane hydrogels with water contents varying from 24 to 38%. For hydrogels with a water content of 38%, the modulus is lower and the rate of change in modulus is slower with respect to

the ratio of NVP to DMA, compared with hydrogels with lower water contents. This lower rate of change in modulus for high-water silicone hydrogels is very favorable because more NVP can be incorporated into the formulation to give potentially better wettability while maintaining low modulus.

Table IV lists formulations derived from $M_2D_{25}/$ TRIS and varying amounts of NVP/DMA, along with key properties of hydrogel films prepared from these formulations. Similar to what was observed from those derived from IDS3H/TRIS/NVP/DMA, the water content and oxygen permeability were maintained at the same level while the modulus dropped dramatically. Figure 5 further illustrates the relationship of both water and tensile modulus to the amount of DMA in the combined NVP/DMA cohydrophilic monomers at 40 parts.

The above formulation studies on silicone hydrogels based on IDS3H and M_2D_{25} showed that the mechanical properties of a silicone hydrogel can be manipulated by varying the ratio of NVP to DMA while keeping water content and oxygen permeability constant. Even more important, a large amount of NVP can be used in a silicone hydrogel formulation while keeping the modulus as low as a material that contains DMA alone. These observations were found to be universal for hydrogels derived from any acrylic-based polysiloxane prepolymer and NVP/DMA as the cohydrophilic monomers.

Surface Wettability and Clinical Performance of Silicone Hydrogels with NVP and DMA

Although no quantitative measure was applied, silicone hydrogel films based on IDS3H/TRIS/NVP were very lubricious and very wettable by appearance, as opposed to comparable hydrogels derived from DMA. Selected formulations based on IDS3H and M_2D_{25} , and with NVP/DMA at 30/10 and 0/40, (listed in Tables III and IV) were cast-molded into lenses using a polar plastic mold. These hydrogel lenses were evaluated clinically, with the results shown in Table V. Initially, they all showed excellent wettability. After 4–6 h of wear, the surface wettability of lenses with NVP remained very good, with only very low levels of lipid deposits on lenses. This is very different from lenses derived from DMA alone, which showed poor wettability and very high levels of lipid deposits.

CONCLUSION

The combination of two hydrophilic monomers, DMA and NVP, in formulations containing poly-

siloxanes produced silicone hydrogels with properties which can be manipulated by varying the ratios of these two monomers. It was shown that high levels of NVP can be used to maintain excellent wettability when used with DMA while maintaining the levels of water content, oxygen permeability, and low modulus.

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