# Novel Polyurethane Hydrogels for Biomedical Applications

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**SYNOPSIS**

Polyurethane hydrogels derived from UV-curable urethane prepolymer and hydrophilic monomers were prepared and their properties were evaluated. The urethane prepolymer used in this study contained well-defined hard segments centered with a polyether-based soft segment and end-capped with methacrylate groups. The hydrophilic monomers studied were 2-hydroxyethyl methacrylate (HEMA), *N*-vinyl pyrrolidone, and glycerol methacrylate. Methacryloxypropyl tris(trimethysiloxy)silane (TRIS) was also used in some cases to modify properties. All compositions were UV-cured and formed hydrogels after hydration. The oxygen permeabilities of the hydrogels decreased as the water contents increased and increased as the TRIS content was increased. The tear strengths and moduli decreased as the water contents of the hydrogels increased. Most compositions studied have higher oxygen permeability and tear strength than poly(HEMA) because of the presence of urethane prepolymer in the composition.

## INTRODUCTION

Polyurethanes have broad applicability because their properties can be tailored by variation of their components: the diol chain extender, the flexible polyol, and the polyisocyanate. Urethane polymers have been used as foams, coatings, adhesives, elastomers, and fibers.[1] Polyurethanes are the most important polymers used in biomedical devices. Presently, over 35 million pounds are being consumed in this area and rapid growth is expected.[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 acrylates by polymerizing diacrylates in the presence of hydrophilic polyurethanes.[4–7] These systems also formed hydrogels and were claimed to have applications as contact lens[5] and surgical implants.[8]

Radiation-curable urethane prepolymers were prepared from flexible polyols and diisocyanates and end-capped with methacrylate or acrylate groups. These were found to have application as coatings.[9] These prepolymers did not have well-defined hard segments and were not as tough as urethane prepolymers with well-defined hard segments.[10]

UV-curable urethane prepolymers derived from several diisocyanates, short chain diols, and poly(propylene glycol)s of various molecular weights were studied and described elsewhere.[11] Polyurethane hydrogels derived from such prepolymers and hydrophilic monomers are described in this paper. Their suitability for ophthalmic applications was evaluated.

## EXPERIMENTAL

### Materials

The synthesis of urethane prepolymer, INP4H, which was derived from isophorone diisocyanate, neopentyl glycol, poly(propylene glycol) of $M_n$ 4000 and end-capped with HEMA, has been described elsewhere.[11]

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The monomers, HEMA, *N*-vinylpyrrolidone (NVP), and glycerol methacrylate (GM), were purified by distillation under reduced pressure. Allyl methacrylate (from Polysciences) and methacryloxylpropyl tris(trimethylsiloxy)silane (TRIS, from Silar) were used as received. Benzoin methyl ether (BME) was purified by recrystallization from methanol.

### Preparations of Hydrogel Films

The urethane prepolymer and hydrophilic monomer were mixed neat or dissolved in toluene with 0.2–0.5% BME added. When NVP was used, 1% of its weight of allyl methacrylate and *t*-butyl peroxyoctoate were also added. TRIS was included in some compositions.

The mix was placed between 10 × 8 cm Pyrex glass plates and cured under a longwave (365 nm) UV lamp (from UVP Inc.) for 2 h. Heat post-cure at 45°C for 1 h was also applied for NVP-containing compositions. The film thickness was controlled by a Teflon gasket material which gave a consistent thickness of 0.25 mm. The films were extracted with toluene, dried, reextracted with boiling water, and then swollen to equilibrium in buffered saline (pH 7.4).

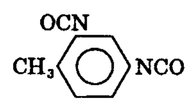
### Characterizations of Hydrogel Films

Mechanical testing was conducted in buffered saline on an Instron instrument utilizing modified ASTM D-1708 (tensile) and D-1938 (tear) procedures. Values are 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. The oxygen permeabilities were measured by the one chamber method[12] with consideration of edge effects and probe configuration and were reported in units of Dk (Dk = $10^{-11}$ cm$^2$ mL $O_2$/s mL mm Hg). The water contents were measured gravimetrically. The contact angles were measured by air-bubble method in buffered saline. The hydrolytic stability determination is described elsewhere.[13] The lysozyme uptake test was done by shaking the 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.

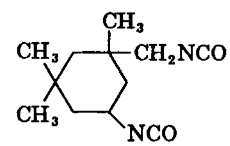
## RESULTS AND DISCUSSION

### The Urethane Prepolymer

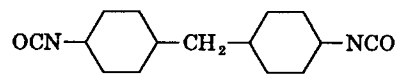
The synthesis and characterization of UV-curable urethane prepolymers with hard–soft–hard blocks were described in a separate paper.[11] These prepolymers were prepared using toluene-2,4-diisocyanate, **1**, isophorone diisocyanate (IPDI), **2**, and bis-(4-isocyanatocyclohexyl) methane, **3**, as the diisocyanates:




TDI, **1**

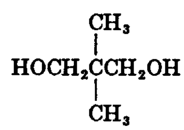



IPDI, **2**

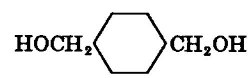



$H_{12}$MDI, **3**

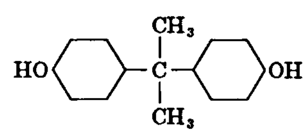
Neopentyl glycol (NPG), **4**, 1,4-dihydroxymethyl cyclohexane, **5**, and hydrogenated bisphenol-A, **6**, were used as the short chain diols and polypropylene glycols of molecular weight 1000 to 4000 as the flexible diols:




NPG, **4**



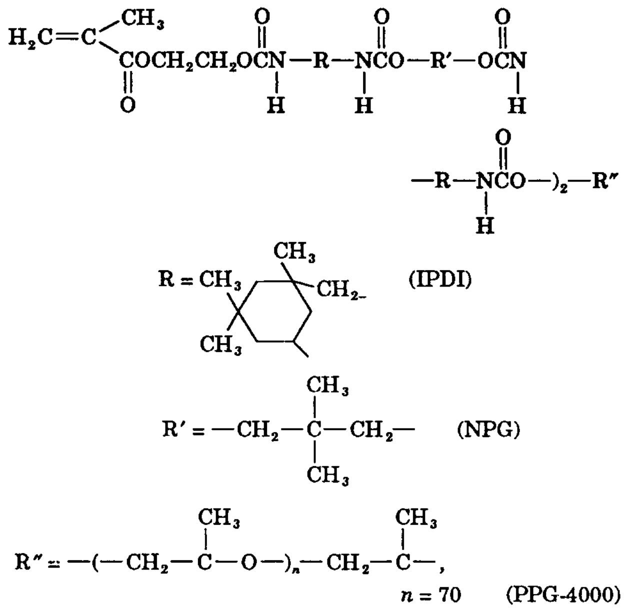

CHDM, **5**




HBPA, **6**

The properties of the cured films cover a wide range. For example, oxygen permeability ranges from 1 to 33 DK and modulus ranges from 190 to 33,000 g/mm$^2$ (1.86–324 MPa). However, all cured films have very good tear strengths (over 39 g/mm or 0.038 kN/m) and have wettable surfaces, with contact angles between 30° and 50°. These values are in the proper range to provide useful hydrogel materials for contact lens applications.

Initial screening[11] of the urethane prepolymers for ophthalmic applications uncovered the INP4H prepolymer, prepared from IPDI, NPG, PPG-4000, and end-capped with HEMA. The structure of this prepolymer is shown below:

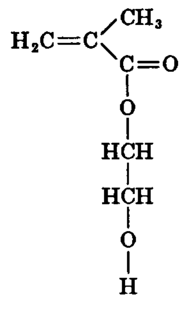


INP4H appeared to be the prepolymer with the best combination of properties for a new contact lens hydrogel material.

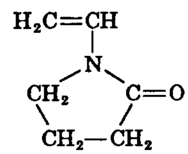
## Preparation of Hydrogel Films

Hydrophilic monomers such as HEMA, **7**, and NVP, **8**, once cured, absorb water and form hydrogels. It is well known that oxygen permeability of common soft hydrogel lens materials depends almost solely on the water content of the hydrogel material; the higher the water content, the higher the oxygen permeability. Poly(HEMA) hydrogel, with a water content of 38%, is the most well-known material for contact lens applications. It is not highly oxygen permeable, but its overall properties for the contact lens application are still unsurpassed by any other hydrogel material. Thus, it serves as the benchmark for comparison of the performance of new hydrogel materials for contact lens applications.

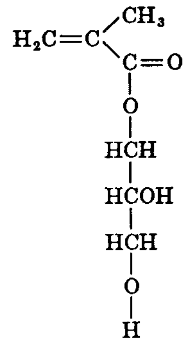
The hydrophilic monomers, HEMA, NVP and GM, **9**, were cured with the INP4H urethane prepolymer to form hydrogels after hydration:



HEMA, **7**

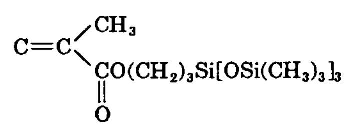


NVP, **8**



GM, **9**

The curing of these methacrylate-capped monomers utilized BME as the initiator. In some compositions containing higher INP4H content, the use of toluene as solvent was preferred to obtain films for characterization. TRIS, **10**, has been used extensively in rigid gas permeable lens because it gives high oxygen permeability due to the presence of bulky siloxane groups[14]:



**10**

Hydrogel films containing varying amounts of TRIS were also prepared to study its effect on oxygen per-

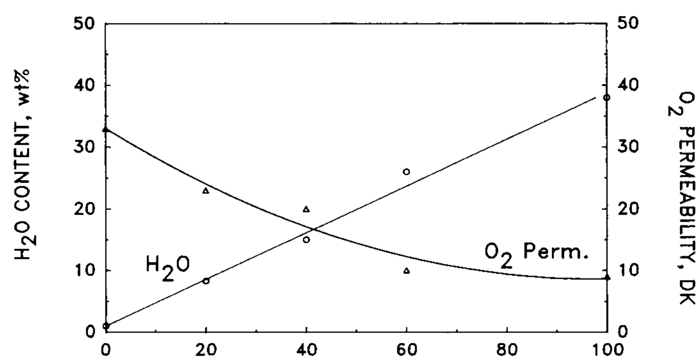



**Figure 1** The relationship of water content and oxygen permeability to HEMA content in INP4H/HEMA hydrogels.

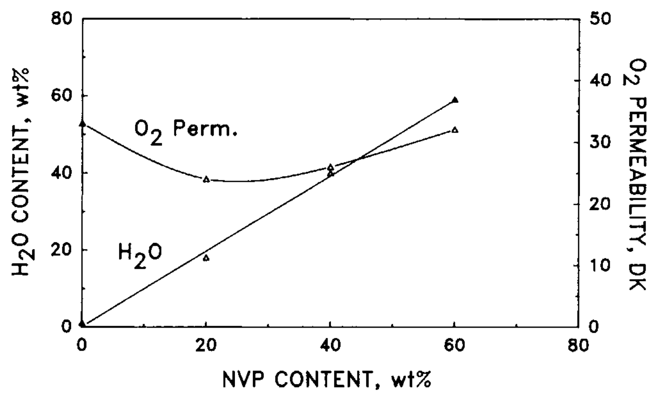



**Figure 2** The relationship of water content and oxygen permeability with NVP content in INP4H/NVP hydrogels.

meability as well as the effect on mechanical properties.

## Water Content and Oxygen Permeability

Figure 1 shows the effect of wt % content of HEMA in the monomer mix on the water content and oxygen permeability of the hydrogel films. As expected, the higher the HEMA content, the higher the water content of hydrogel. However, the oxygen permeability decreases as HEMA or water content increases. This is contrary to what has been normally observed for hydrogels. The reason for this discrepancy is that the hydrogels derived from hydrophilic monomers normally used in ophthalmic application impart oxygen permeability solely from the water content and their dry films are not oxygen permeable. However, the dry, cured urethane prepolymer films have reasonable oxygen permeability (e.g., oxygen permeability is 33 in Dk units). Thus the oxygen permeability in INP4H/HEMA hydrogels was the result of the cured urethane prepolymer rather than the water content and the values are always higher than that of HEMA hydrogel regardless the amount of HEMA in the INP4H/HEMA hydrogels. The oxygen permeability of poly(HEMA) hydrogel, with water content of 38%, is only 9 Dk units.

When a monomer with a higher hydrophilicity than HEMA was used to copolymerize with the INP4H urethane prepolymer, the contribution of oxygen permeability from water is higher because of higher water content. For example, when NVP was used instead of HEMA, the hydrogel films contained 1% water per percentage increase of NVP, as shown in Figure 2. The oxygen permeability decreased from 33 to 24 as NVP content was increased from 0 to 20%, but it reversed to 32 when the NVP content was increased to 60%. This also suggests that the oxygen permeabilities of the hydrogels remained relatively unchanged over a rather wide range of NVP content (from 0 to 60%) as shown in Figure 2. It can be envisioned that other hydrophilic monomers with similar hydrophilicity, such as *N,N*-dimethyl acrylamide and *N*-vinyl-*N*-methylacetamide, would exhibit a similar relationship between oxygen permeability/water content and hydrophilic monomer content.

When TRIS was included in the INP4H/HEMA compositions, with the HEMA content fixed at 20% by weight and thus the same low water content (9%) for the hydrogel, the Dk values increased as the amount of TRIS was increased (Fig. 3). A cured neat TRIS film has oxygen permeability over 200 Dk units. These silicone-containing hydrogels also showed different water content-oxygen permeability

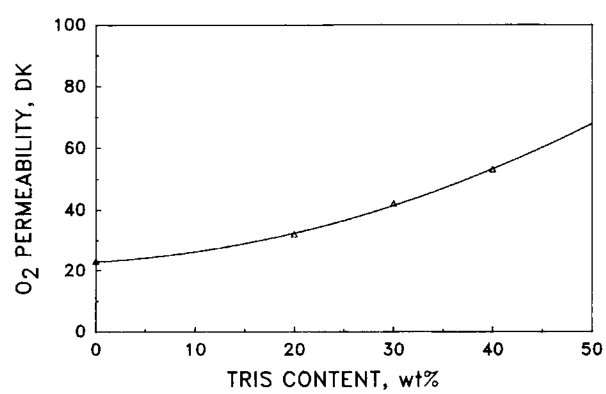



**Figure 3** The relationship of oxygen permeability with TRIS content in INP4H/TRIS/HEMA hydrogels (with HEMA content at 20%).

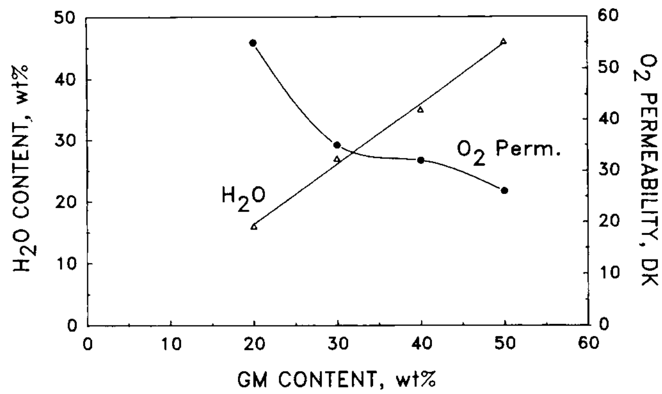



**Figure 4** The relationship of water content and oxygen permeability with GM content in INP4H/TRIS/GM hydrogels with constant INP4H content (40 wt %).

relationships when the water content is higher. For example, in hydrogel films derived from INP4H/TRIS/GM, the oxygen permeability decreased as the TRIS content decreased even though the water content increased as shown in Figure 4.

## Contact Angle and Wettability

For hydrogels to be useful as contact lenses, they must be wettable. Although it is not always applicable, determination of the contact angle of the hydrogel films is still the most meaningful *in vitro* test for surface wettability. The contact angles of the polyurethane hydrogels prepared in this study were in the range of 30–40°, which is the same as poly(HEMA) hydrogel.

## Protein Absorption

One of the critical factors for a polymeric material to be considered for biomedical applications is its interaction with the biosubstrate. Polyurethane materials useful for implants should not absorb protein from the blood; otherwise thrombosis can occur. Similarly, for polymeric 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

**Table I Lysozyme Uptake of Hydrogels**

| Composition (Feed) | Trade Name (Product) | Water (%) | Lysozyme Uptake (μg/mg) |
|---|---|---|---|
| Poly(HEMA) | Soflens | 38 | 0–1 |
| Poly(HEMA-*co*-MAA)[a] | B & L 58 | 58 | 25 |
| 98/2 | Vistamac | | |
| Poly(MMA-*co*-NVP)[b] | B & L 70 | 70 | 4 |
| Polyurethanes | | | |
| INP4H/HEMA | | | |
| 60/40 | | 16 | 0 |
| INP4H/TRIS/HEMA | | | |
| 40/40/20 | | 9 | 0 |
| INP4H/TRIS/GM | | | |
| 40/40/20 | | 16 | 0 |
| INP4H/NVP | | | |
| 60/40 | | 40 | 0 |
| 40/60 | | 59 | 0 |

[a] MAA = methacrylic acid.
[b] MMA = methyl methacrylate.

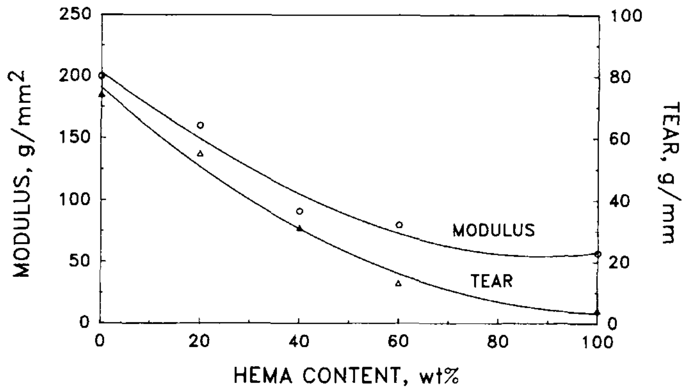



**Figure 5** The relationship of tear strength and modulus with HEMA content in INP4H/HEMA hydrogels.

can adversely effect the performance of the contact lens and could ultimately lead to ocular disease.

Poly(HEMA) hydrogels do not pick up any significant amounts of lysozyme. Table I illustrates some lysozyme uptake data of the polyurethane hydrogels as well as those of some established soft contact lens products for comparison. Regardless of the water content, all the polyurethane hydrogels prepared in this study have insignificant lysozyme uptake and are essentially equivalent to poly(HEMA) hydrogels. The hydrogel, poly(HEMA-*co*-MAA), has a very high lysozyme uptake.

## Mechanical Properties

Figure 5 illustrates the relationships of modulus and tear strength with HEMA content in INP4H/HEMA hydrogels. As expected, the modulus decreased from 200 g/mm$^2$ (1.96 MPa) to 80 g/mm$^2$ (0.78 MPa) as the HEMA content was varied from 0 to 60%. Similarly the tear strength decreased as the content of HEMA was increased.

Figure 6 illustrates the relationships of modulus/tear strength versus NVP content in INP4H/NVP hydrogels, whereas Figure 7 shows the same relationships for INP4H/GM/TRIS (with a constant INP4H content) hydrogels. In both series similar trends are demonstrated as the INP4H/HEMA series. That is, as the relative amount of hydrophilic monomer increased, the tear strength and modulus decreased. It is worthwhile to note that, except for some hydrogels with water content higher than 38%, the tear strengths and moduli of polyurethane hydrogels are far higher than those of hydrogels currently used for ophthalmic applications. Hydrogels with higher tear strength implies that the medical device fabricated from it is more durable. However, any clinical advantage of higher modulus of the hydrogel material remains to be evaluated.

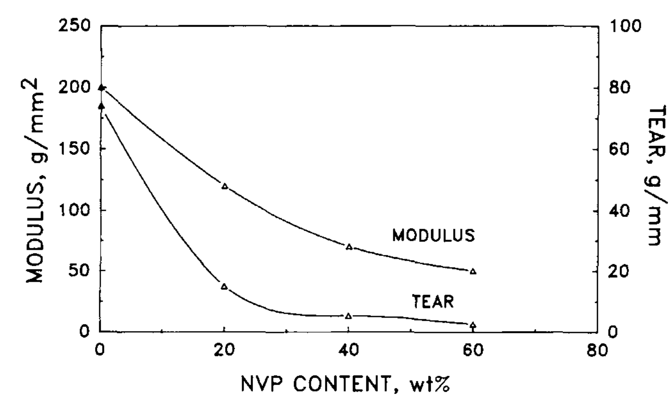



**Figure 6** The relationship of tear strength and modulus with NVP content in INP4H/NVP hydrogels.

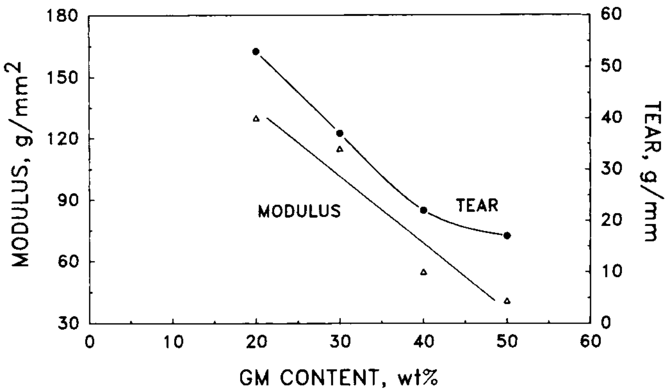



**Figure 7** The relationship of tear strength and modulus with GM content in INP4H/TRIS/GM hydrogels with constant INP4H content (40 wt %).

## CONCLUSION

UV-curable compositions of urethane prepolymers and hydrophilic monomers can be used to form hydrogels. These hydrogels have excellent mechanical properties and much better oxygen permeability than poly(HEMA) hydrogel. These hydrogels may be useful as contact lens materials and other biomedical devices.

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