Effect of Crosslinkers on Photocopolymerization of *N*-Vinylpyrrolidone and Methacrylates to Give Hydrogels

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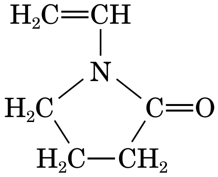
ABSTRACT: *N*-Vinylpyrrolidone (NVP) and methacrylates are frequently copolymerized to give hydrogels useful as contact lenses. However, the nature of their copolymerization was not well understood. In this study, the effect of a crosslinker on the photocopolymerization of NVP and 2-hydroxyethyl methacrylate (HEMA) was discussed. It was found that crosslinkers with a vinyl carbonate group can copolymerize with NVP better than those containing an allyl group, which, in turn, are better than those containing a methacrylate group. A crosslinker with a vinyl carbonate and a methacrylate group can copolymerize NVP and HEMA the best in terms of giving hydrogels with the highest water content, followed by a crosslinker with a combination of allyl and methacrylate groups. Crosslinkers with only methacrylate or vinyl carbonate groups gave hydrogels either too fragile or too stiff to be useful. © 1997 John Wiley & Sons, Inc. J Appl Polym Sci **66:** 1475–1484, 1997

INTRODUCTION

It is known that methacrylates and *N*-vinylpyrrolidone (NVP, **1**) do not copolymerize well. For example, the reactivity ratios for the copolymerization of methyl methacrylate (MMA, as monomer 1) and NVP (as monomer 2)[1] are $r_1 = 5$ and $r_2 = 0.02$. Copolymers of NVP and methacrylates, such as 2-hydroxyethyl methacrylate (HEMA, **2**), are mostly known in the form of hydrogels and are used in many applications in the biomedical area, especially in contact lenses. Copolymers of this type have been prepared via thermal or a combination of photo- and thermal polymerization, using ethylene glycol dimethacrylate (EGDMA, **3**) or other methacrylates as the crosslinker[2]:



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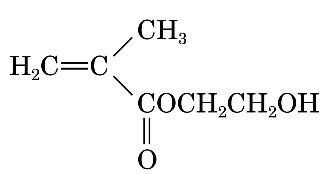

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It is also known that all lens materials derived from NVP also contain methacrylates. There are good reasons for combining methacrylates and NVP together for making hydrogel lenses. These include the high polarity/hydrophilicity of NVP, thus giving high water hydrogels. However, the mechanism for their copolymerization is far from clear. To address these issues, a series of basic studies were conducted. In this article, the effect of crosslinkers on the photocopolymerization of a methacrylate and NVP and the properties of hydrogels derived were reported, using the photocopolymerization of HEMA and NVP as an example.

EXPERIMENTAL

Monomers, Crosslinkers, Initiator, and Solvents

NVP was distilled under reduced pressure and stored under nitrogen at room temperature with potassium hydroxide pellets. Methacryloxyethyl vinyl carbonate and ethylene glycol divinyl carbonate were prepared by procedures described elsewhere.[3,4] HEMA (with 0.02% of EGDMA, Optical Monomers Inc.), 2-hydroxy-2,2-dimethyl acetophenone (Darocur-1173, EM Industries), and glycerine (Aldrich) were used as received. Benzoin methyl ether (BME) was recrystallized from methanol.

Film Preparations

The monomer mixes containing HEMA, NVP, crosslinkers, glycerine, and 0.2% Darocur-1173 were prepared. The amount of diluent (glycerine) used was 25% of the weight of the mix. The mix was introduced between two glass plates (10×8 cm) and cured under a long-wave UV lamp (from UVP, intensity 4000 microwatts per cm^2) for 2 h. The film thickness was controlled by a Teflon gasket material which gave fairly consistent thicknesses of 0.25 mm. The films were extracted with boiling water for 4 h and then swollen to equilibrium in a phosphate-buffered saline (pH 7.30).

Characterization of Polyvinylpyrrolidone

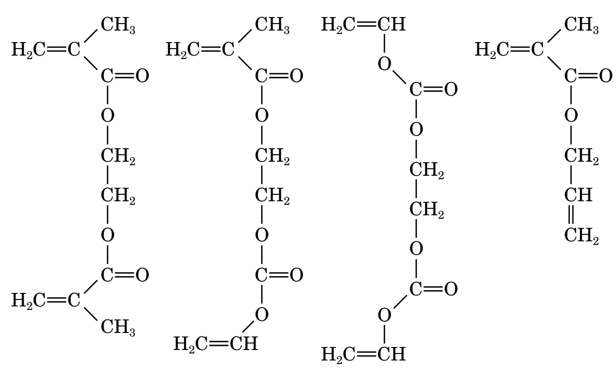
For a monomer mix containing NVP, but without a crosslinker, the film, as polymerized, using the same procedure as described, was dissolved in water and characterized for molecular weight by size-exclusion chromatography.

Characterization of Hydrogel Films

Mechanical testing was conducted in buffered saline on an Instron instrument, according to a modified ASTM D-1708 (tensile) procedure and were reported in g/mm^2 for the tensile modulus. The water extractables of films as cured and water contents of hydrogels were determined gravimetrically.

RESULTS AND DISCUSSION

To understand the copolymerization of HEMA and NVP, it is desirable to understand the homopolymerization of HEMA and NVP. It was demonstrated previously that a novel crosslinker methacryloxyethyl vinyl carbonate (HEMAVC, **4**, MW 200), which has both methacrylate and vinyl carbonate groups, can copolymerize well with both methacrylate and NVP.[5] In this study, crosslinkers with different combinations of polymerizable groups—methacrylate and vinyl carbonate—but of the same molecular weight, were compared for the copolymerization of HEMA and NVP. They were EGDMA (MW 198), HEMAVC, and ethylene glycol divinyl carbonate (EGDVC, **5**, MW 202). It should be noted here that, because HEMAVC, EGDMA, and EGDVC have similar molecular weight, when they were used at the same weight percent the mol percent is nearly the same. In addition to those three crosslinkers, allyl methacrylate (AMA, **6**, MN 136) was also used for comparison:



3 **4** **5** **6**

To focus on the discussion of the crosslinker, only 2-hydroxy-2,2-dimethyl acetophenone (Darocur-1173) at 0.2% was used as the initiator and glycer-

Table I Photopolymerization of HEMA

Initiator	Diluent	EGDMA (%)	Extract (%)	Water (%)
0.2 BME	No	0.02	9.0	40.8
0.2 BME	Glycerine	0.02	1.0	37.5
0.2 Dar	No	0.02	3.4	39.1
0.2 Dar	Glycerine	0.02	0.9	37.1
0.2 Dar	No	0.1	3.4	37.8
0.2 Dar	Glycerine	0.1	2.5	39.5

[a] Dar, Darocur-1173.

Table II Photopolymerization of NVP

Run No.	Initiator[a]	Diluent	Appearance of Film
1	0.2 BME	No	Viscous liquid
2	0.2 BME	Glycerine	Tough film
3	0.2 Dar	No	Brittle film
4	0.2 Dar	Glycerine	Tough film

[a] Dar, Darocur-1173.

ine at 25% was used as the solvent unless otherwise specified.

Homopolymerizations of HEMA and NVP

Polymerization of HEMA

Because EGDMA is the most frequently used crosslinker for HEMA, it was the only one used for curing HEMA in this study. The HEMA used contained 0.02% EGDMA and this was the purest HEMA that we could obtain. Thus, HEMA-based formulations containing different levels of the crosslinker EGDMA (0.02, 0.1, 0.2, and 0.4% of HEMA weight) were polymerized, using either BME or Darocur-1173 at 0.2%.

Table I lists the results from this study. Surprisingly, HEMA gave a well-cured polymer having low extractables with EGDMA at 0.02%. One would expect that, normally, a soluble, linear material would be obtained at this low level of a crosslinker. Based on this study, it would be extremely difficult to obtain linear HEMA polymer, if not totally impossible. The results of low (less than 3.5%) water extractables of dry films indicated little difference among cured films regardless of crosslinker and diluent content, except when HEMA was cured under UV, with BME and low crosslinker (0.02%) content. The water contents, as high as 40%, are relatively independent of curing conditions, but decreased as the crosslinker content was increased. The hydrogel films were clear. The effect of the nature of initiators and diluents and their concentrations on the polymerization of HEMA was the subject of a separate publication.[6]

Polymerization of NVP

Table II lists the NVP formulations used in polymerization and the appearance of films as polymerized. Table III summarizes the results of the molecular weight measurement of poly(*N*-vinylpyrrolidone) (PVP) by size-exclusion chromatography and the distribution of polymer, oligomers, and residual NVP. Please note that no average molecular weight of PVP can be obtained in most examples due to heterogeneity in the molecular weight distribution. From this study, it was found that

1. Without a crosslinker, NVP polymerized to give water-soluble polymers of different molecular weights.
2. NVP polymerized better in glycerine than in neat (in terms of molecular weight and distribution of polymerized fragments).

Effect of Crosslinker in the Curing of NVP

Although the amount of crosslinkers used in any hydrogel seldom exceeds 2% by weight, to under-

Table III Molecular Weight of PVP Under Different Polymerization Conditions

		Distribution[a]			
Sample No.	M_n	Area 1	Area 2	Area 3	Total
1	51K	0.504	—	0.571	1.075
2	70K	0.786	0.206	—	0.923
3	68K	0.939	0.147	0.092	1.178
4	85K	0.929	0.238	—	1.168

See Table IV for sample identifications.
[a] Area 1 represents high molecular weight PVP; area 2, oligomers of NVP; and area 3, NVP.

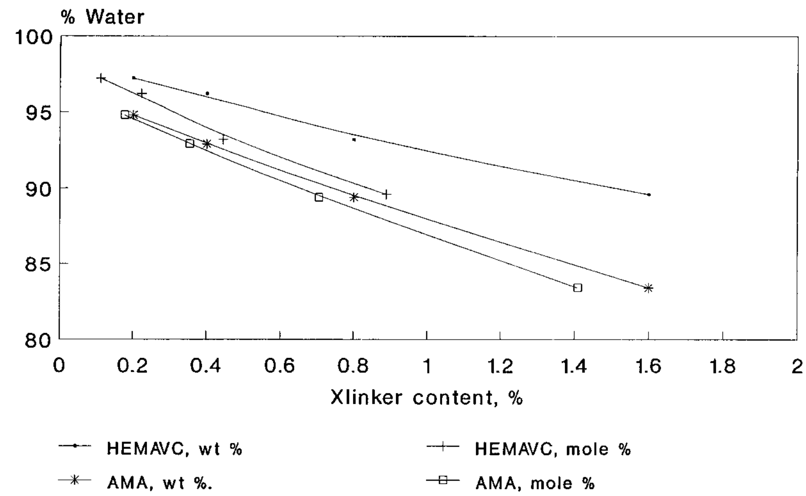


Figure 1 Water content versus crosslinker content for PVP hydrogels (HEMAVC and AMA up to 2%).

stand the effect of crosslinker on NVP-based hydrogel films, the amount of crosslinker (HEMAVC, AMA, EGDMA, EGDVC) used ranged from 0.2 to 51.2% of the weight of NVP. All formulations were cured under the same UV conditions and processed into hydrogel films.

The comparison of HEMAVC and AMA in a water content at low crosslinker concentration (up to 1.6% by weight) is further depicted in Figure 1. In general, on a weight basis, AMA gave hydrogel films with lower water contents when compared to HEMAVC. This is mainly due to higher crosslinking density with AMA. A smaller difference in the water content of the hydrogel was observed when these two crosslinkers were compared on a molar basis. When the water content–crosslinker content relationship was further extended to a higher crosslinker concentration studied (up to 20–25 wt or mol %) as shown in Figure 2, it also showed the same trend in the difference in the water content when the same moles of HEMAVC or AMA was used as the crosslinker. The likely cause for their difference could be the difference in morphology triggered by the difference in the molecular weight of the crosslinkers.

Figure 3 shows a comparison of EGDVC with HEMAVC in the relationship between the water content and the crosslinker. EGDVC consistently gives hydrogels with a higher water content, indi-

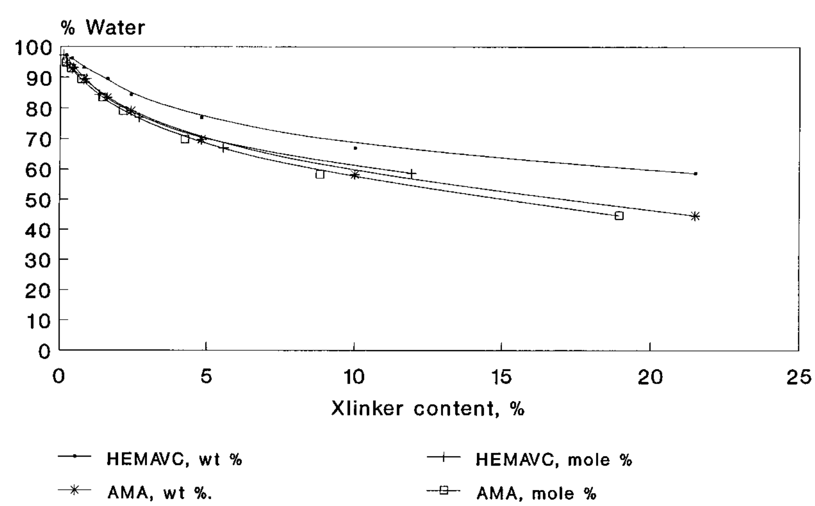


Figure 2 Water content versus crosslinker content for PVP hydrogels (HEMAVC and AMA up to 24%).

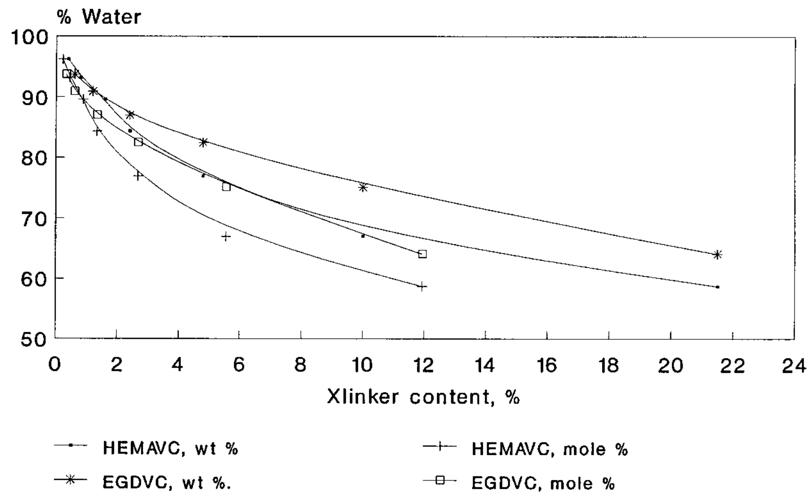


Figure 3 Water content versus crosslinker content for PVP hydrogels (HEMAVC and EGDVC up to 24%).

cating that vinyl carbonate can copolymerize NVP better than can a methacrylate group, as expected.

Figure 4 shows a comparison of EGDMA with HEMAVC in terms of the water content of the hydrogels obtained. As expected, HEMAVC consistently gave NVP-based hydrogels with a higher water content, again indicating that a vinyl carbonate group can copolymerize NVP better than can a methacrylate group.

Figure 5 gives a total comparison of all crosslinkers under study. On a weight basis, the ability of incorporating NVP decreases in the order of EGDVC, HEMAVC, AMA, and EGDMA.

Are Methacrylates (EGDMA) Good Crosslinkers for NVP?

EGDMA has been used frequently in crosslinked polymer networks containing NVP. Is EGDMA a good crosslinker for NVP? To understand this, NVP and EGDMA with different weight ratios (and molar ratios) of methacrylate to vinyl groups were cured under UV. The films obtained were characterized for solubility in boiling water or water content if a hydrogel was obtained. The results of this study are summarized in Table IV. It was found that, when up to 1.6% of EGDMA was used, the polymerized products were totally water-solu-

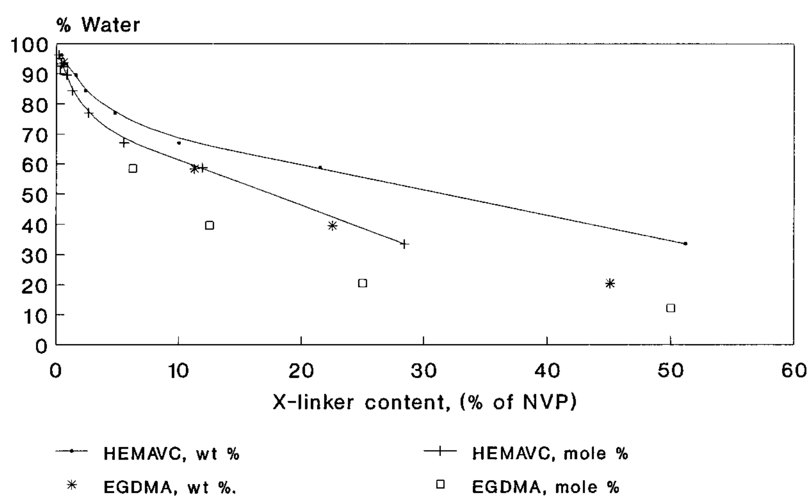


Figure 4 Water content versus crosslinker content for PVP hydrogels (HEMAVC and EGDMA up to 50%).

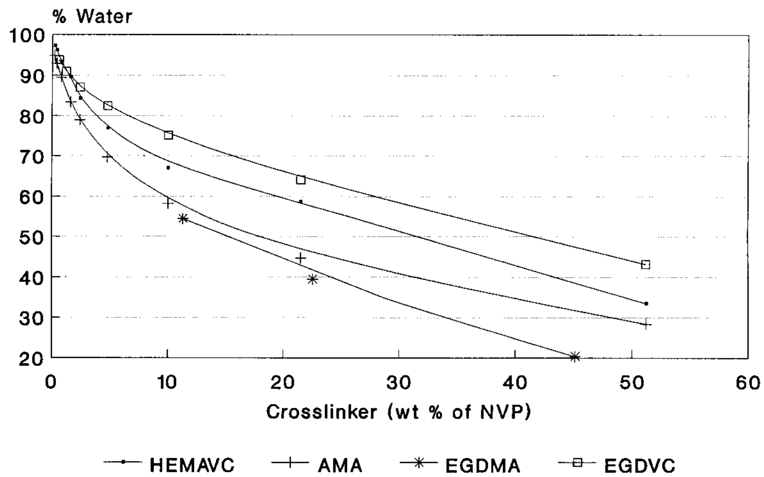


Figure 5 Water content versus crosslinker content for PVP hydrogels (all crosslinkers up to 50%).

ble upon boiling, indicating that EGDMA is not an effective crosslinker for NVP curing when compared to other crosslinkers such as HEMAVC or EGDVC. Because of the wide difference in reactivity, during the copolymerization of NVP and methacrylates, including EGDMA, all methacrylate groups are used up before a significant number NVP molecules can incorporate with a methacrylate such as EGDMA.

When a higher amount of EGDMA was used, stiff hydrogel films with a water content of 58% or less could be obtained. The nitrogen contents of dry polymers (with 5.6% EGDMA or more) were identical to the calculated values (although the measured values were still consistently lower than were the calculated values by less than 1 percentage point) (Table V). These results indicated that the cured polymers derived from NVP and EGDMA did have the right composition of NVP in the polymer when the amount of EGDMA used was sufficient, regardless of a lack of understanding of the mechanism of copolymerization. The water content of the hydrogels with EGDMA as a crosslinker were, however, consistently lower than when using HEMAVC and EGDVC as the crosslinker, as shown in Figure 5.

Table IV Curing of NVP with EGDMA in Glycerine (25%) with 0.2% Darocur-1173 (Formulation: NVP/EGDMA/Glycerine/Darocur-1173)

EGDMA/NVP Ratio				
Molar[a]	Wt Ratio	Cured Film	Hydrated Film	% Water
2 : 1	1.804 : 1	Stiff, cracked yellow[b]	Stiff, colorless fine pieces	5.9
1 : 1	0.902 : 1	Stiff, cracked yellow[b]	Stiff, colorless pieces	12
1 : 2	0.451 : 1	Stiff, cracked yellow[b]	Stiff, colorless, not broken	20
1 : 4	0.225 : 1	Brittle, light yellow	Hazy, colorless, not broken, hydrogel	39.5
1 : 8	0.113 : 1	Tough, colorless	Hazy hydrogel	58.4
1 : 16	0.0564 : 1	Tough, colorless	Broken into fine pieces[d]	[c]
1 : 32	0.0282 : 1	Tough, colorless	Broken into fine pieces[d]	[c]
1 : 55	0.016 : 1	Tough, colorless	Water-soluble	[c]
1 : 110	0.008 : 1	Tough, colorless	Water-soluble	[c]
1 : 220	0.004 : 1	Tough, colorless	Water-soluble	[c]
1 : 440	0.002 : 1	Tough, colorless	Water-soluble	[c]

[a] Molar ratio of vinyl groups to methacrylate groups.
[b] Some glycerine was in a separate phase.
[c] Cannot be measured for obvious reasons.
[d] Lost a lot of weight, but cannot be measured properly.

Table V Elemental Analyses of NVP/EGDMA-Cured Samples

Sample from EGDMA/NVP with Feed Vinyl/ Methacrylate Ratio[a]	Nitrogen Content (%)	
	Actual	Theoretical
2 : 1 (1.801 : 1)	4.03	4.50
1 : 1 (0.902 : 1)	6.47	6.67
1 : 2 (0.451 : 1)	8.16	8.80
1 : 4 (0.225 : 1)	9.86	10.39
1 : 8 (0.1128 : 1)	10.75	11.37
1 : 16 (0.0564 : 1)	10.79	11.95

[a] Molar ratio, followed by weight ratio shown in parentheses.

When the molar ratio of vinyl to methacrylate was changed from 55 : 1 to 32 : 1, some NVP repeating units in the polymer products were crosslinked by EGDMA or self-crosslinking occurred. However, no shaped hydrogel pieces could be collected. When the molar ratio was changed from 4 : 1 to 8 : 1, they formed hazy-to-opaque hydrogels, with water contents somewhere between 40 and 60%.

Photocopolymerization of HEMA and NVP

From an application point of view, the main purpose of combining NVP with a methacrylate, such as HEMA or methyl methacrylate, was to make high water hydrogels useful as contact lens. Thus, it was not appropriate to use a crosslinker which was not capable of copolymerizing with NVP. As such, in this study, the weight ratio of the HEMA and NVP used was geared toward high water hydrogels, with the weight ratios of HEMA to NVP ranging from 70/30 to 30/70, targeting hydrogels with water contents of 50% and more. The crosslinkers used in this study ranged from 0.2 to 1.6% by weight of HEMA and NVP combined. The parameters for comparing these crosslinkers were percent water extractables of the cured films and the water contents and mechanical properties of the hydrogels. The percent extractables is an indication of how well HEMA and NVP were copolymerized through the crosslinker. The water content is an indication of how well NVP was incorporated into the cured films. Mechanical properties give a clue as to how NVP and HEMA are combined together, which are also a reflection of water content.

Table VI gives the results of percent extractables and water contents for formulations based on HEMA/NVP at 70/30 and 30/70. As expected, a higher crosslinker concentration led to lower extractables, indicating that both HEMA and NVP were incorporated better. However, among the crosslinkers used, HEMAVC and AMA gave cured films with much lower extractables, because they contained two different polymerizable groups which can copolymerize better with either HEMA or NVP. On the other hand, EGDMA can copoly-

Table VI Effect of Crosslinker on Percent Extractables and Water Content for HEMA/NVP/ Crosslinker at 70/30/x and 30/70/x (x = 1.6 or 0.8)

		Property			
		Extractables (%)		Water (%)	
		HEMA/NVP			
Crosslinker	Weight Percent	70/30	30/70	70/30	30/70
HEMAVC	1.6	0.7	2.8	54.7	78.9
	0.8	5.3	5.9	59.0	85.6
EGDMA	1.6	4.5	20.0	50.9	72.7
	0.8	6.4	23.8	54.6	78.5
AMA	1.6	0.3	3.6	51.6	75.9
	0.8	4.4	6.0	58.6	81.5
EGDVC	1.6	4.0	12.4	60.2	86.2
	0.8	7.5	14.0	66.8	90.6
No		19	[a]	83.0	[a]

[a] Unable to obtain.

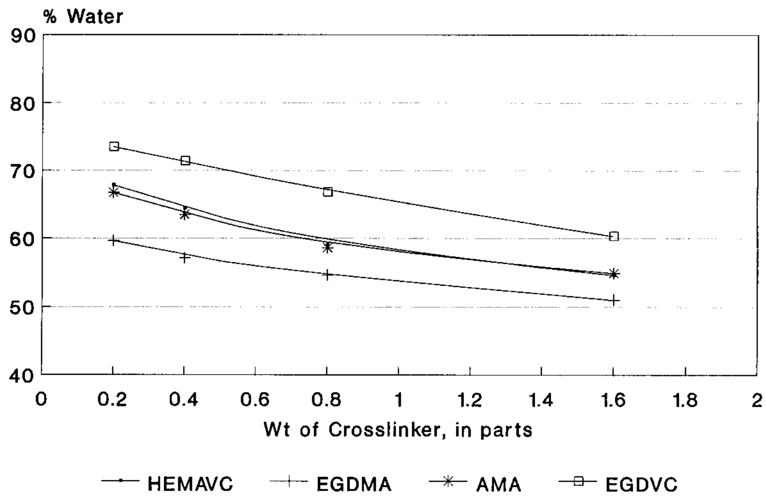


Figure 6 Water content versus crosslinker content for HEMA/NVP at 70/30.

merize better with a methacrylate–HEMA, but not with NVP, and EGDVC can copolymerize better with NVP, but not with a methacrylate. Thus, they gave cured films with higher extractables. For a water content of hydrogels derived from HMEA/NVP, it was interesting to note that, without a crosslinker (except the 0.02% EGDMA in the HEMA monomer used), for HEMA/NVP at 70/30, the cured films became gummy upon hydration, with a water content over 80%, indicating that NVP, to a large degree, cured by itself. The cured film had a high extractable (19%). For HEMA/NVP with a 30/70 weight ratio, without a crosslinker, the film formed broke into fine pieces upon hydration. In formulations with a crosslinker, it was found that EGDMA gave hydrogels with the lowest water content, AMA and HEMAVC gave hydrogels with a water content of intermediate range, and EGDVC gave hydrogels with the highest amount of water, indicating that EGDMA incorporates more HEMA and EGDVC incorporates more NVP, while HEMAVC and AMA incorporate both monomers well. This indicated that EGDVC incorporates better with NVP, with more HEMA lost, thus giving hydrogels with a higher water content. EGDMA incorporates better with HEMA, with more loss of NVP, thus giving hydrogels with a lower water content. AMA and HEMAVC gave films with the same low level of extractables and the same medium level of water content in the hydrogels.

The water content versus crosslinker relationship is further depicted in Figures 6–8 for hydrogels based on HEMA/NVP at 70/30, 60/40, and 30/70, respectively. The difference in water content can be as high as 20% points by changing the

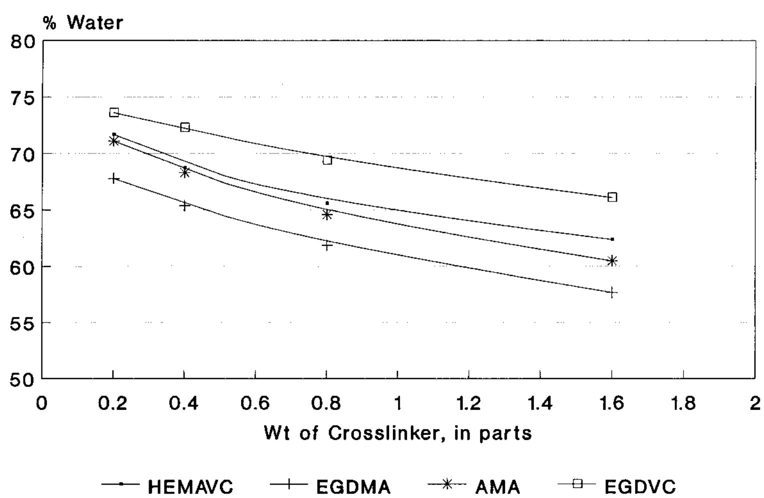


Figure 7 Water content versus crosslinker content for HEMA/NVP at 60/40.

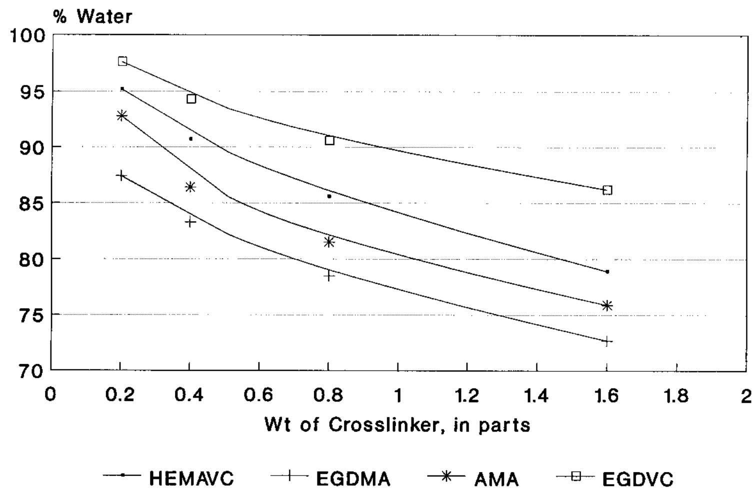


Figure 8 Water content versus crosslinker content for HEMA/NVP at 30/70.

crosslinker concentration from 0.2 to 1.6%. In all cases, EGDVC gave hydrogel films derived from all compositions with the highest water content, followed by HEMAVC and then AMA. EGDMA gave hydrogels with the lowest water content.

Mechanical properties are crucial for application of a hydrogel. Particularly, tensile modulus and tear strength are two important properties of hydrogels for their application as contact lens. Figure 9 shows the relationship between modulus and crosslinker concentration for a formulation based on HEMA/NVP at 70/30. The hydrogel films crosslinked with EGDVC were so heterogeneous (and weak as well) that no mechanical properties could be measured. In general, the higher the crosslinker concentration, the higher the modulus. HEMAVC gave hydrogels which were much softer than EGDMA would, indicating that HEMAVC behaves differently as compared to EGDMA as a crosslinker. The difference in modulus was also partly caused by the difference in water content. HEMAVC and AMA gave hydrogel films with the same modulus even though they had different copolymerizability toward NVP.

Figure 10 gives the same relationships for hydrogels derived from HEMA/NVP at 30/70. Because of a high water content and the ability of incorporating more NVP, EGDVC gave hydrogels which were very fragile. As a result, only the formulation cured with 1.6% EGDVC could be measured for the modulus (at less than 10 g/mm^2). As expected, EGDMA gave cured films with the highest modulus, followed by AMA and then HEMAVC.

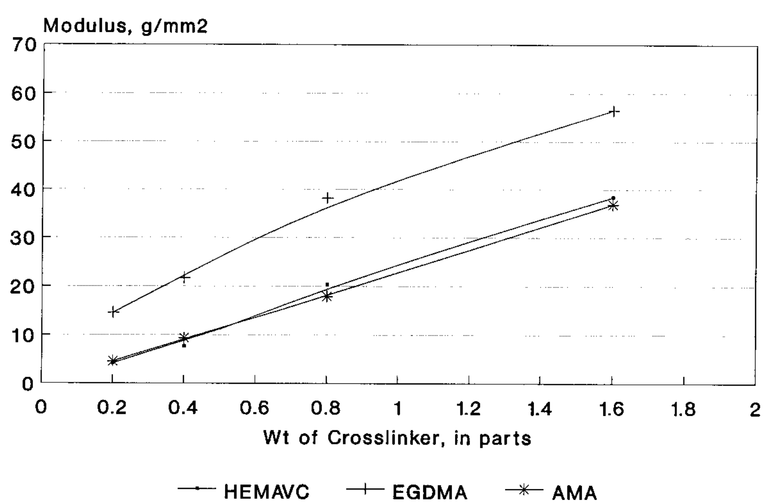


Figure 9 Tensile modulus versus crosslinker content for HEMA/NVP at 70/30.

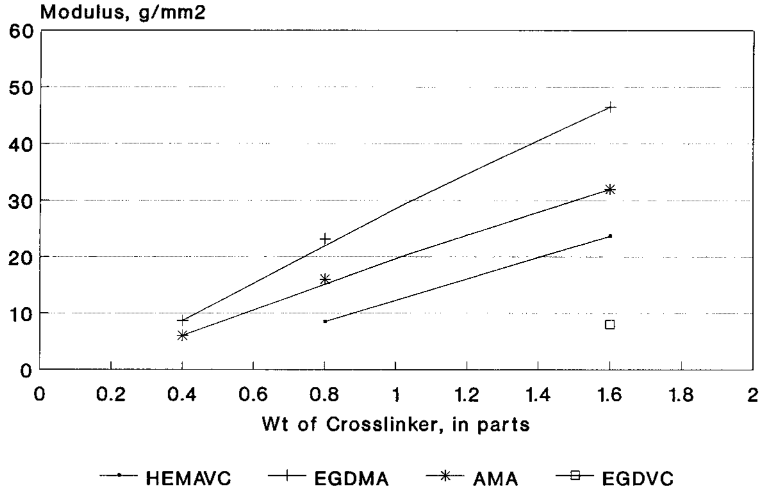


Figure 10 Tensile modulus versus crosslinker content for HEMA/NVP at 30/70.

It should be noted here that, by comparing formulations based on HEMA/NVP at 70/30 and 30/70 and cured with HEMAVC or AMA, AMA and HEMAVC worked equally well in incorporating HEMA and NVP when the formulation contains more HEMA than NVP. However, HEMAVC gave hydrogels with a lower modulus and higher water content for formulations containing more NVP than HEMA, indicating that HEMAVC indeed copolymerizes NVP better than does AMA. This difference is important in obtaining high water hydrogels.

Based on the results obtained from the curing of HEMA, NVP, and HEMA/NVP, there are some similarities and some differences in terms of the role of a crosslinker. The similarity was that HEMAVC and AMA work equally well for curing either NVP or HEMA/NVP. The difference was that EGDMA works better for copolymerizing HEMA/NVP, but was not good enough in curing NVP. On the other hand, EGDVC works well in curing NVP, but not good enough as a crosslinker for HEMA/NVP.

CONCLUSION

EGDMA was not an effective crosslinker for NVP. It gave NVP/methacrylate-based hydrogels with a substantially lower water content compared to HEMAVC, a crosslinker with both a methacrylate and a vinyl carbonate. EGDVC, a vinyl carbonate-based crosslinker, could cure NVP well, but did not serve well for the copolymerization of NVP and methacrylates, which gave hydrogels with poor mechanical properties. HEMAVC and AMA could incorporate both HEMA and NVP well and work equally well for the copolymerization of a formulation containing more HEMA and less NVP. However, HEMAVC worked better than AMA for formulations containing more NVP and less HEMA.

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