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High strength poly(meth)acrylamide copolymer hydrogels

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Summary.

The hydrogels described here are copolymers of acrylamide and methacrylamide highly cross-linked with piperazine diacrylamide or 4,7,10-trioxa-1,13-tridecanediamine diacrylamide by radical polymerisation in highly concentrated aqueous and aqueous gelatin solutions. The hydrogels were characterised by their compressive strength, refractive indices, densities, 'free' water contents and degree of swelling. The hydrogels cross-linked with piperazine diacrylamide gave strong glassy hydrogels, which we have termed "hydroglasses". Cross-linking with 4,7,10-trioxa-1,13-tridecanediamine diacrylamide, which contains a long flexible spacer, did not result in a more elastic gel. Polymerisation in an aqueous gelatin solution improved the mechanical properties of the gel enormously.

Introduction.

The aim of this work was to synthesise a relatively strong hydrogel with a high refractive index which could find use as a contact or intraocular lens. The synthesis and properties of hydrogels, especially the heterogeneity of polyacrylamide gels, has been the subject of many studies [1-12]. In order to synthesise gels with a high optical refractive index and good clarity which could be used in a watery environment we have used high concentrations of cross-linker and comonomer (60 weight%) which results in a low water uptake. Another advantage of these high concentrations is that an increase in the monomer concentration reduces the chance that a polymer radical encounters a pendant double bond on its own chain instead of a monomer which would lead to cyclisation reactions and thus a more heterogeneous network [13]. Increasing the cross-linker concentration gives a stronger network, whereas a lower initiator concentration increases phase separation and inhomogeneity [14]. The criteria for a strong hydrogel from a molecular point of view are homogeneity, low water uptake and the absence of loops and dangling ends. A homogeneous hydrogel is a network with random fluctuations in density. During the synthesis of the network, micro gel particles (gel balls) which give strongly cross-linked particles in the networks should not be formed [15]. Loops and dangling ends do not contribute to the strength of the hydrogel because they are not load-bearing. The hydrogels have been characterised by their compressive strength, refractive indices, densities, 'free' water contents and degree of swelling.

This paper describes the synthesis of a hydrogel made from a copolymer of acrylamide (AAm) and methacrylamide (MAAm) cross-linked with piperazine diacrylamide (PDA) by means of radical polymerisation in solution. Polyacrylamide is a very hydrophilic polymer and so methacrylamide is added to make the hydrogel less hydrophilic in order to decrease the water uptake and thus to strengthen the hydrogel. PDA is known to be a cross-linker which gives relatively strong PAAm gels [16,17], using PDA in our experiments resulted in a strong and glassy but brittle hydrogel which we have termed a "hydroglass".

To overcome this brittleness we synthesised a new cross-linking agent, 4,7,10-trioxa-1,13-tridecanediamine diacrylamide (TTDDDA) which contains a long flexible spacer.

The monomer reactivity ratios for acrylamide and methacrylamide are $r_1=0.74 \pm 0.11$ and $r_2=1.1 \pm 0.2$ respectively [18] giving a random copolymer. So heterogeneities in the network could not be on account of the polyacrylamide-polymethacrylamide phase separation.

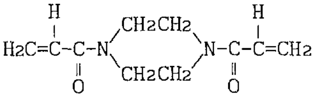
When the polymerisation takes place in a gelatin solution, the initiation of the copolymerisation of a AAm, MAm and PDA mixture leads to the formation of a PAAm and PMAm copolymer network trapping the gelatin chains within. This is the semi interpenetrating network (semi-IPN) state [10,11,19], with ultimate strengths higher than the homopolymer network. This is in line with the results of Chatterji [10,11] who polymerised acrylamide/bisacrylamide mixtures in a gelatin solution and measured their strength in the dry state. In general, semi-IPN's are microphase separated materials with improved toughness compared with the homopolymer network [19].

Experimental.

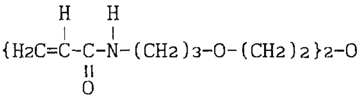
Materials.

Acrylamide (AAm) was supplied by Serva, methacrylamide (MAAm), ammonium persulphate (per), 4,7,10-trioxa-1,13-tridecanediamine and acryloylchloride by Aldrich, piperazine diacrylamide (PDA) by Biorad and gelatin by UCB. AAm and MAAm were recrystallised from toluene, acryloylchloride was distilled under reduced pressure and 4,7,10-trioxa-1,13-tridecanediamine, PDA, gelatin and per were used as supplied.

piperazine diacrylamide (PDA):



4,7,10-trioxa-1,13-tridecane-diamine diacrylamide (TTDDDA):



$\{H_2C{=}\overset{H}{C}{-}\underset{\overset{\|}{O}}{C}{-}\overset{H}{N}{-}(CH_2)_3{-}O{-}(CH_2)_2\}_2{-}O$

Synthesis of 4,7,10-trioxa-1,13-tridecanediaminediacrylamide (TTDDA).

22 g (100 mmole) of 4,7,10-trioxa-1,13-tridecanediamine was dissolved in 400 ml chloroform and 22 g (268 mmole) of sodium acetate was added to it. The solution was cooled to 0 °C and 17.9 ml (220 mmole) of acryloylchloride in 20 ml chloroform was added, slowly keeping the temperature below 5 °C. The solution was stirred for an hour at room temperature, followed by the addition of 150 mg of hydroquinone. The solution was then refluxed for 1.5 hours , cooled and filtered. The solvent was evaporated and the residue was recrystallised twice from acetone. Yield 60 %, melting point 57 °C, ^{1}H NMR (250 MHz.) in $CDCl_3$; NH: 6.9 ppm,

$H_2C{=}\underline{CH}$: 6.1 ppm, $H_2C{=}\underline{CH}$: 5.5 ppm, CH_2O: 3.6 ppm, CH_2N; 3.4 ppm and $CH_2\underline{CH_2}CH_2$: 1.8 ppm.

Preparation of the hydrogels.

AAm and MAAm in a mole ratio of 3:7 and a total weight of 2 g were introduced in a test tube with a diameter of 16 mm PDA (2.5-10 mole%) was added to the mixture after which the test tube was sealed with a septum and flushed with nitrogen. To this was added 40 weight% distilled and degassed water to set the monomer concentration at 60 weight%. A thermocouple connected to a recorder was used to measure the temperature during the polymerisation. The mixture formed a homogeneous solution at 55 °C. The system was initiated by addition of an aqueous solution of ammonium persulphate (0.05 mole%, based on the total amount of double bonds). The polymerisation was ended when the temperature, as measured with the thermocouple, reached a peak due to the exothermic effect. A typical example of the amounts used is 0.528 g (7.42 mmole) AAm, 1.472 g (17.3 mmole) MAAm, 0.360 g (1.854 mmole = 7.5 mole%) PDA, 1.47 ml water and 0.1 ml (3.24 mg/0.1 ml.) ammonium persulphate solution. All polymerisations were checked for reproducibility.

Instead of PDA, TTDDDA was also used as cross-linking agent in a concentration of 7.5 mole%. The same procedure was used to prepare the hydrogels in a gelatin solution. Instead of water, a warm gelatin solution (5 and 10% by weight) was used. The PDA concentration in this case was varied from 0 to 7.5 mole%.

Density measurements.

The densities of the hydrogels were determined in their hydrated states. The sample was weighted in air and in water at a known temperature. The difference in weight is a measure of the volume of the sample.

Equilibrium degree of swelling q.

The equilibrium degree of swelling q was approximated as follows. The weight of the swollen gel was determined after swelling for three days in an excess of water. The weight of the dry state of the gel was directly obtained from the concentration of the reactants in the freshly synthesised gel, assuming complete conversion. The ratio of these two weights gave the equilibrium degree of swelling.

Compressive measurements.

Compressive measurements were carried out on an Instron 4301 universal testing machine. The samples without gelatin were measured in their hydrated states, while the ones with gelatin were measured in their synthesised states using a load cell of 5 kN. Measurements were performed at room temperature and at 50 °C. The samples were cylindrical with a diameter of approximately 18 mm and a length of approximately 15 mm.

Refractive index.

Approximations of the refractive indices were determined as follows. The clear samples were abraded with sandpaper. These samples were immersed into solvents of known refractive indices. If the sample became clear, then the refractive indices of the solvent and the sample could be assumed to be equal.

'Free' water content.

Thermograms were obtained from a hydrated sample using a Perkin-Elmer differential scanning calorimeter, DSC-7. The 7-14 mg samples were cooled to -50 °C and allowed to reach thermal equilibrium. The samples were then heated to 90 °C at a rate of 10 °C/min. The 'free' water content was calculated by using the standard value of the melting enthalpy of water (334 J/g) [20, 21].

Results and discussion.

Polymerisation.

The hydrogels were synthesised by means of radical polymerisation in solution. The solution contained 60 weight% monomer (AAm and MAAm in a mole ratio of 3:7 and 2.5-10 mole% PDA) and 40 weight% degassed distilled water. The polymerisation was performed at 55 °C and initiated by 0.05 mole% ammonium persulphate (based on the total amount of double bonds) in solution.

As the polymerisations began, the solutions were slightly opaque for a short period of time, but at the gel point (during the exothermic effect), they turned transparent. This effect appeared even when no cross-linker was added. The polymerisation time increased from 10 to 20 minutes when the cross-linker concentration was decreased from 10 to 2.5 mole%. The maximum amount of MAAm that could be incorporated into the polymer was 70 mole% on account of its solubility in water. The polymerisation with TTDDDA as cross-linking agent and polymerisation in the pale yellow gelatin solution gave similar results.

At the gelpoint, the temperature could rise from 55 °C to far above 100 °C in 30 seconds due to the exothermic effect. The temperature must not rise above 100°C in order to prevent boiling of the solvent. This can be realised by decreasing the monomer concentration, the concentration of the cross-linker, the initiator concentration or the polymerisation temperature. It has been chosen to control the exothermic effect by changing the polymerisation temperature because decreasing the other parameters leads to a weaker or more heterogeneous network, [13, 14]. A lower polymerisation temperature increases the polymerisation time and leads to a smaller exothermic effect.

Equilibrium swelling degree of the hydrogels with PDA as cross-linker.

The higher degree of cross-linking prevents swelling of the network as shown in Figure 1. The degree of swelling is 1.66 in the synthesised state. The equilibrium degree of swelling decreases from 2.78 to 1.89 with an increase in the cross-linker concentration from 2.5 to 10 mole%.

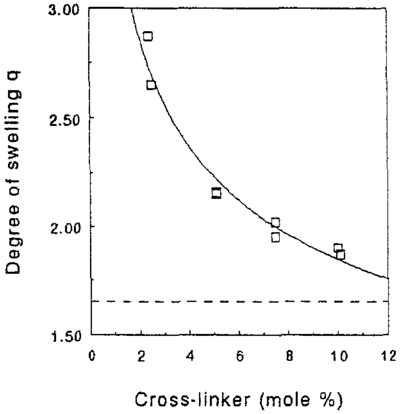


Figure 1: *The equilibrium degree of swelling versus the piperazinediaacrylamide concentration for the hydrogel which consists of a network of acrylamide-methacrylamide-copolymer with a comonomer ratio of 3:7.*

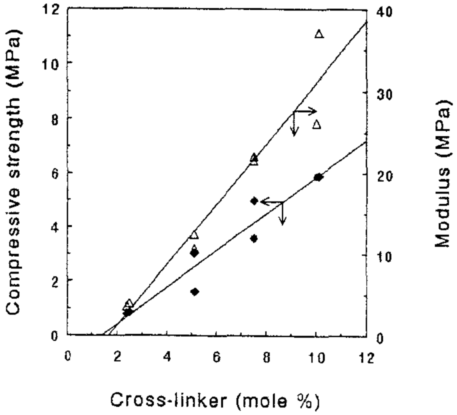


Figure 2: *The compressive strength and modulus versus the piperazine diacrylamide concentration for the hydrogel which consists of a network of acrylamide-methacrylamide copolymer with a comonomer ratio of 3:7.*

Compressive strength measurements of the hydrogels with PDA.

The maximum deformation of compressed samples without gelatin in their hydrated states was about 20 % after which they showed brittle fracture. Figure 2 shows that the compressive strength increases linearly from 0.8 MPa to 6.1 MPa and the modulus increases linearly from 4 MPa to 31 MPa with an increase in the concentration of the cross-linker from 2.5% to 10%. Compared with the widely used hydrogel polyhydroxyethylmethacrylate (polyHEMA) which contains less water and has a tensile strength of 0.5 MPa and a modulus of 0.25 MPa [21], the hydrogels described above show excellent mechanical properties.

The hydrogel was glassy and hard; hard enough to be abraded with sandpaper so that they could be termed "hydroglasses" instead of hydrogels. The hydrogels containing less than 10 mole% of cross-linker were completely transparent. The exothermic effect of the hydrogel containing 10 mole% PDA was hard to control and so the hydrogel prepared from 7.5 mole% cross-linker was the toughest transparent hydrogel prepared. Some characteristics of this hydrogel were determined.

Characteristics of a PDA hydrogel.

The characteristics of hydrogels which consists of a network of acrylamide-methacrylamide-copolymer with a comonomer ratio of 3:7 and 7.5 mole% PDA are listed in Table 1. It was not possible to measure the refractive indices with the Abbe refractometer because thin regular sheets of hydrated hydrogel were difficult to prepare. The abraded sample was slightly visible in chlorobenzene (n_D= 1.542) and benzaldehyde (n_D= 1.544), but invisible in acetophenone (n_D= 1.538), so that the hydrated polymer could be assumed to have a refractive index of approximately 1.53.

Water in polymers can exist in more than one state. These states are called 'bound' (through hydrogen bonding) and 'free' or freezing water. The properties of a hydrogel are therefore determined by the degree of swelling q and by the ratio of freezing to non-freezing water. The amount of 'free' water in a hydrogel can be determined by DSC [20,21]. In this way it was found that in our PDA hydrogels a large percentage (91%) of water is attached to the hydrogel by means of hydrogen bonding. This indicates a small quantity of 'free' water which is an indication of the macroscopic homogeneity of the hydrogel. This was also confirmed by SEM and AFM micrographs of the hydrogel which showed a smooth fracture surface on a µm. scale.

Characteristics of a TTDDA hydrogel.

Hydrogels which consists of a network of acrylamide-methacrylamide-copolymer with a comonomer ratio 3:7 and 7.5 mole% TTDDDA showed a compressive strength of 0.45 MPa and a modulus of 2.9 MPa. The equilibrium degree of swelling was 2.35 and brittle fracture was observed after 15% deformation. This cross-linker with the long flexible spacer and a more reactive double bound did not give the expected improvement in toughness [9,22] but led to a brittle hydroglass with even poorer mechanical properties than the hydroglasses cross-linked with PDA. This may be due to enhanced cyclisation reactions [22] or a difference in crosslink distribution [23]. An improvement in mechanical properties was obtained by polymerisation in a gelatin solution.

Compressive measurements of the PDA hydrogels with gelatin.

The maximum strength of hydrogels measured in their synthesised states containing 2 and 4 weight% gelatin exceeded 25 MPa and could not be measured because the breaking load of the samples exceeded the maximum load of the 5 KN load cell. This load was reached at 20-40% strain depending on the concentration of PDA. The moduli of the gels which contain 4 weight% gelatin were 30, 130 and 480 MPa for 0, 2.5 and 7.5 mole% PDA respectively. The gels containing 2 weight% gelatin and 7.5 mole% PDA showed a modulus of 300 MPa. The samples returned completely to their original state on removal of the load. Figure 3 shows the stress-strain curves for samples with 2.5 mole% PDA and 4 weight% gelatin, and 5 mole% PDA without gelatin. It shows that the modulus and strength increase enormously when gelatin is incorporated in the network.

A warm aqueous solution of gelatin sets to a gel upon cooling because inter- and intrachain hydrogen bonds are formed [10,11,21]. To obtain information about the nature of the improvement the following experiment was performed. The temperature of compressive measurement was increased to 50 ^{0}C, which is above the dissolution temperature of a gelatin gel (37 ^{0}C) [24]. Such an increase in temperature did not result in a decrease in modulus. This indicates that the incorporated gelatin had not set to a gel upon cooling. In contrast with the other gels, the samples containing gelatin changed from clear yellow to a phase-separated white and became brittle and lost their strength upon immersion in water.

Table 1: *Characteristics of the equilibrium swollen hydrogels which consists of a network of acrylamide-methacrylamide-copolymer with a comonomer ratio of 3:7 and 7.5 mole% piperazine diacrylamide.*

Equilibrium degree of swelling q	1.98	
Compressive strength	4.3	MPa
Modulus	21.9	MPa
Deformation at break	20	%
Refractive index	1.53 ± 0.01	
'free' water content	9	%
Density hydrogel	1.18	g/cm^3

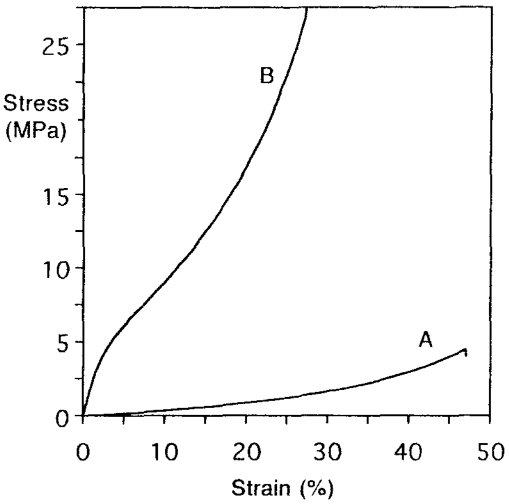


Figure 3: *Stress-strain curves for samples containing 40 weight% water and 60 weight% network of acrylamide-methacrylamide-copolymer with a comonomer ratio 3:7 and (A) without gelatin and 5.0 mole% piperazine diacrylamide and (B) 4.0 weight% gelatin and 2.5 mole% piperazine diacrylamide.*

Conclusions.

This paper describes the synthesis of a new hydrogel, containing a network of acrylamide-methacrylamide-copolymer with a comonomer ratio 3:7 and 2.5-10 mole% piperazine diacrylamide (PDA). The strong exothermic effect during polymerisation can be controlled by changing the polymerisation temperature, a lower polymerisation temperature leading to a smaller exothermic effect. The hardest transparent hydrogel consisted of a network of acrylamide-methacrylamide-copolymer with a comonomer ratio 3:7 and 7.5 mole% PDA and had an equilibrium degree of swelling of 1.98. This hydrogel is glassy and hard enough to be abraded. It has a compressive strength of 4.3 MPa, a modulus of 21.9 MPa which is relatively high for hydrogels. One can compress these to 20 % in the hydrated state before they show brittle fracture, so they could be termed "hydroglasses". For a water swellable polymer they have a very high refractive index of 1.53 ± 0.01, so they can find use as an optical element in a watery environment, for example as an intraocular lens for cataract patients. A large percentage (91%) of water is attached to the hydrogel by means of hydrogen bonding. This indicates a small quantity of 'free' water which is an indication of the macroscopic homogeneity of the hydrogel.

If 7.5 mole% 4,7,10-trioxa-1,13-tridecanediamine diacrylamide (TTDDDA) is used as cross-linking agent instead of PDA, the equilibrium swelling degree is only slightly higher and they also showed an early brittle fracture; these TTDDDA gels are also hydroglasses. Surprisingly, the compressive strength and modulus drops by a factor of almost 10.

When the PDA hydrogel contains 4 weight% gelatin, the modulus of the gel as measured in its synthesised state, increases enormously. The modulus does not change when the temperature of the measurement is increased to 50 ^{0}C, which means that the incorporated gelatin has not set to a gel on cooling. When the hydrogels with gelatin are immersed in water, they become white and brittle and lose their strength.

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