

Synthesis and characterization of amphiphilic networks obtained by copolymerization of poly(ethylene oxide) macromonomers with methyl methacrylate

Géraldine Carrot, Bertrand Schmitt, Pierre Lutz*

Institut Charles Sadron (CNRS-ULP), 6, rue Boussingault, F-67083 Strasbourg, France

Received: 18 December 1997/Revised version: 15 January 1998/Accepted: 15 January 1998

Summary

Hydrogels whose elastic chains are constituted of hydrophilic Poly(ethylene oxide) (PEO) segments were obtained through free radical homopolymerization or copolymerization with methylmethacrylate (MMA) of α,ω -methacryloyloxy PEO macromonomers. This reaction can be conducted in water solution or in organic solvent. These networks were investigated as gels swollen to equilibrium in THF or in water. The influence of the preparation solvent on the properties of these networks was studied. The mechanical properties of the networks obtained in water are better than those of networks obtained under exactly the same conditions in organic solvents. This result can be explained by the preferential formation in water of micellar structures containing a higher concentration of polymerizable units. The influence of the concentration of the hydrophobic comonomer on the properties of these PEO networks was also examined.

Introduction

Poly(ethylene oxide), (PEO) is a hydrophilic polymer which exhibits specific solution and solid state properties (1). Furthermore, the remarkable biocompatible properties of PEO have already led to a wide number of biomedical applications (2,3). Much interest has been devoted to the preparation and the study of hydrogels based on PEO. These networks are usually prepared by end-linking PEO chains fitted at both chain ends with hydroxyl functions with a plurifunctional isocyanate (4). The presence of these pluriisocyanate derivatives in the gel may not be the best solution for hydrogels designed for biomedical applications. In addition, that reaction has to be conducted in organic solvents. The purpose of the present work is to present and discuss the extension of a new preparation method of hydrogels, by homopolymerization of bifunctional PEO macromonomers (5), to the synthesis of amphiphilic networks. The first part of this work deals with a discussion on the influence of increasing concentrations of hydrophobic comonomer on the properties of the networks. The influence of the polymerization solvent on these properties (amount of extractable material, equilibrium swelling degree, uniaxial compression modulus) will also be examined. The second part concerns a kinetic study of the network formation process.

* Corresponding author

Experimental

Macromonomer synthesis

A commercially available α -hydro, ω -hydroxy PEO of molar mass 2940 g/mol was first treated, according to well established procedures, to remove remaining protonic impurities (6). In a second step, that PEO is reacted, under inert atmosphere, with a stoichiometric amount of diphenylmethyl potassium to transform quantitatively the end groups of the PEO into alcoholates. These living ends were then deactivated with methacryloyl chloride according to a method described previously (6). The resulting macromonomer is recovered by precipitation and characterized.

Network formation procedure.

The free radical polymerization or copolymerization of these macromonomers was carried out in water (potassium persulfate being the initiator) or in benzene (with α , α' azo-isobutyronitrile) at a temperature of 65°C. The initiator concentration was kept by one molar percent per methacrylate unit. Different reaction times have been selected. After formation, the networks are placed in a great excess of the selected swelling solvent (THF or water). These solvents are exchanged until no polymer is present. The amount of extractable materials is given directly by the weight of polymer in the solvent.

Network characterization methods

Equilibrium degree of swelling:

The method of determination of the volume degree of swelling of networks (Q_v) has been discussed in detail elsewhere (7). The relationship between the weight equilibrium swelling degree of swelling Q_w and Q_v is:

$$Q_v = 1 + (Q_w - 1) \cdot (\rho_s / \rho_g)$$

where ρ_s and ρ_g are the specific volumes of the solvent and the dry gel respectively.

Uniaxial compression modulus in a solvent medium:

A cylindrical sample was placed between two disks in a solvent bath at a constant temperature of 25°C. The upper disk was attached to a pressure transducer which can be moved by means of a micrometric screw. The lower disk was in a fixed position, below the cell containing the solvent. The corresponding force exerted on the sample by turning the micrometric screw is measured by the transducer (7).

Gels synthesized in water were studied by transmission electron microscopy (Philips EM 300, 100kV or EM 430ST, 300kV). We used microtomed slices cut with diamond knife at room temperature (Reichert-Jung Ultracut E).

Results and discussion

Ito (8) showed that for the homopolymerization of monofunctional PEO macromonomers, the nature of the solvent directly influences the polymerization: the reaction is much more rapid in water than in organic solvents. According to him, that effect is due to the presence at the chain end of the macromonomer of a hydrophobic end group leading to a self-organization of the PEO macromonomer in aqueous media. That strategy has been extended to the case of bifunctional PEO macromonomers (5) whereby hydrogels could be obtained.

In the present work a hydrophobic comonomer is copolymerized with a PEO macromonomer. As in the case of homopolymerization gel formation occurs. To determine the influence of various experimental parameters, these gels were studied extensively. The first indication to determine the quality of a network is given by the amount of extractable polymer. The lower that content the better the properties of the network. The amount of extractable polymer was also determined for all PEO hydrogels obtained by homopolymerization or by copolymerization in water or in benzene. The results presented on table 1 call for a few comments:

- In homopolymerization as in copolymerization reactions, the amount of extractable material is higher when the reaction is carried out in benzene than in water. This result is coherent with earlier data concerning the homopolymerization of PEO macromonomers (5). As stated in these homopolymerization reactions, a possible explanation may be the formation of micellar structures with domains containing high concentration of polymerizable units. This is in favor of high polymerizable yields. The probability of reaction between polymerizable groups is enhanced, corresponding to an increase of the number of elastic chains. A good argument is also the appearance of the PEO macromonomer solutions: benzene solutions are clear whereas aqueous solutions are opaque. The gels formed subsequently exhibit a quite similar behavior even in the presence of the hydrophobic comonomer and they are characterized by a lower content of extractable polymer.

- In benzene, i.e. in homogenous medium it is well established (9,10) that the radical polymerization of macromonomers is affected by the macromolecular nature of the polymerizable unit leading to slow polymerization. This is directly reflected by the higher amount of extractable materials. In addition, it is observed that these amounts increased also with increasing initial MMA content.

Table 1 Physico-chemical characteristics of PEO gels obtained by homopolymerization or copolymerization with MMA in water (W) or benzene (B)

r	C _{eff}	ε (W)	ε (B)	Q _v water (W)	Q _v THF (B)	σ (Pa), W	σ (Pa), (B)
homo	0.13	6.8	13.0	8.3	9.2	111 000	61 000
1.11	0.14	6.0	13.6	7.7	6.9	122 000	65 000
2.00	0.16	5.5	14.0	7.1	6.5	132 000	76 500
3.33	0.17	3.8	14.5	6.8	6.2	107 000	85 000
10.0	0.20	2.9	15.3	5.8	6.1	98 000	98 500

The initial concentration (total weight concentration of polymerizable species per unit volume of solvent) is 30 weight %, r is the ratio $n_{\text{MMA}} / n_{\text{macro}}$, C_{eff} represents the polymer concentration in the gel at swelling equilibrium (expressed in g/ml).

Equilibrium degree of swelling

Once the extractable materials have been removed from the networks, the gels were swollen to equilibrium either in THF or in water depending upon the preparation solvent. The different values of the equilibrium swelling degrees are given in table 1 and the following comments can be made. For networks obtained under similar conditions, the differences in swelling degrees between water and THF are not very important whatever the preparation solvent. This is attributed to the fact that both solvents can be considered as good solvents for PEO. In addition, swelling degrees are less affected by a modification of structural parameters than the mechanical properties. The values observed for the homopolymeric networks are yet always higher. When increasing concentrations of MMA are incorporated, a systematic decrease of the values is observed. This is especially the case for networks prepared in water. This can be explained by the increased concentration of hydrophobic species. For organic solvents, that decrease may be explained by an increasing number of elastic chains with the increasing MMA content.

Uniaxial compression modulus:

As just discussed, the study of the evolution of the equilibrium swelling degrees is not a very efficient method to determine the influence of various experimental parameters on the properties of these networks. Far better conclusions may be drawn from the uniaxial compression modulus. Two cases have been examined in detail: the influence of increasing concentrations of polymerizable units on the modulus and for a given concentration of polymerizable units the kinetics of the reaction of homo or copolymerization.

The uniaxial compression modulus is given by the following stress/strain relationship:

$$f_{\text{elast}} / Sg = \nu RT \cdot Qg^{1/3} \cdot (\Lambda - (Q/Qg) \Lambda^2)$$

Where f_{elast} is the force applied to the network, $\Lambda = l/l_0$ the compression ratio, l and l_0 are the instantaneous and initial length of the gel. Sg is the cross-section of the dry gel and ν is the density of elastic chains in the network. Q and Q_g are the swelling degrees of the gel under stress and the swollen gel before the stress, respectively. Since the measurements were made instantaneously, we did not take into account a possible deswelling of the gel during compression. Hence $Q = Q_g$ and the gel modulus can be calculated from the slope of the curve: $f_{\text{elast}} / Sg = f(\Lambda - \Lambda^2)$.

Network formation in water

Evolution of the uniaxial compression modulus versus comonomer concentration

As indicated in table 1, for low concentration of (MMA), the values of the uniaxial modulus are slightly higher than in the case of homopolymerization. This can be explained by the incorporation of the hydrophobic comonomer into the hydrophobic domains constituted by the polymerizable chains ends of the PEO macromonomers dissolved in water. Thus the number of junction points are higher and the number of effective elastic chains is increased. When the MMA concentration is still increased, the uniaxial modulus decreases again. This may be due to a modification of the structure of the gel, the comonomer no longer being incorporated into the micelles formed by the macromonomers because of the stronger hydrophilic/hydrophobic forces. This leads to a dispersion of droplets of the hydrophobic MMA in water followed by polymerization. The color changed from a cloudy white to a transparent blue color confirming the presence of microphases. The PMMA chains are trapped in the gel (the fraction of extractable material is still low), they are not connected to the network structure.

Transmission Electron Microscopy (TEM)

This evolution of the structure with increasing content of MMA is confirmed by Transmission Electron Microscope experiments (Figure 1): for low amounts of MMA it is still possible to see the PEO lamellae, the matrix (the PMMA domains are not visible because of the high intensity of the electron beam). When the MMA content is increased to a ratio of 10, the matrix is mainly constituted of PMMA (using a higher contrast and a lower intensity), the smaller domains corresponding to the PEO.

Differential scanning calorimetry (DSC)

When the MMA content is high, a decrease in the “sizes” of the fusion peak and the crystallization peak is observed. This suggests a disruption of the PEO chains. The loss

of regularity in the system is caused by the formation of PMMA. This effect was small compared with that observed in organic media. There was only a slight increase in the glass transition temperature compared to that obtained for gels with PEO only, when the MMA content was high. This suggests the formation of short PMMA chains. Further work has to be done in that domain.

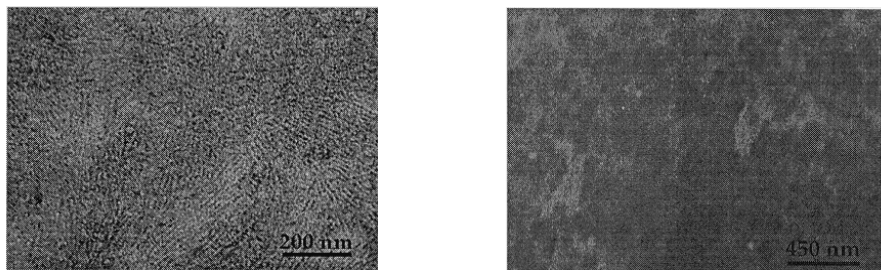


Figure 1. TEM images showing the structural change for the gels synthesized in water, (left) the ratio ($n_{\text{MMA}}/n_{\text{macro}}$) is 1.11. The PEO lamellae size is about 10 nm and the beam intensity is 300 kV. (Right) the ratio is 10 and the beam intensity is 100 kV.

Network formation in benzene

Evolution of the uniaxial compression modulus versus comonomer concentration

The copolymerization was also studied in benzene. Contrary to water, benzene is a good solvent for the macromonomer and miscible with MMA. Thus the reaction can be assimilated to the classical network formation process by free radical copolymerization of a monofunctional monomer with a bifunctional polymerizable compound. During polymerization, the viscosity is high due to the presence of the macromonomers the chain diffusion is slow. MMA, a micromolecular monomer, can diffuse rapidly in that viscous medium.

Therefore, sequences of PMMA could serve as links between the pendant chains, increasing the number of elastic chains and improving the mechanical properties of the network. This was reflected by the monotonic increase in modulus with MMA content.

Differential scanning calorimetry (DSC)

DSC measurements (heating rate 20°C /mn) also showed the copolymerization process to differ from that in water. The DSC traces evidenced the presence of two glass transition temperatures ($t_{g1} = -43^\circ\text{C}$ and $T_{g2} = -20^\circ\text{C}$) indicating the presence of long sequences of PMMA. There were therefore two distinct phases, one containing mainly PEO, the other principally made up of PMMA. The crystallinity was completely disrupted owing to the formation of long sequences of amorphous PMMA. When the amount of MMA is high,

these long chains still participate to the network formation, the PEO macromonomers are now used as a cross-linking agent between PMMA chains. This lead to an improvement of the mechanical properties.

Kinetic study of the gel formation process

K. Ito showed that the propagation rate of amphiphilic macromonomers is higher in aqueous medium than in benzene (9). In water, macromonomers form a viscous medium in which their diffusion process is reduced. The local concentration of polymerizable units is very high. This effect must be stronger in the presence of hydrophobic comonomers. This is confirmed by the evolution of the uniaxial compression modulus (table 2 and figure 2).

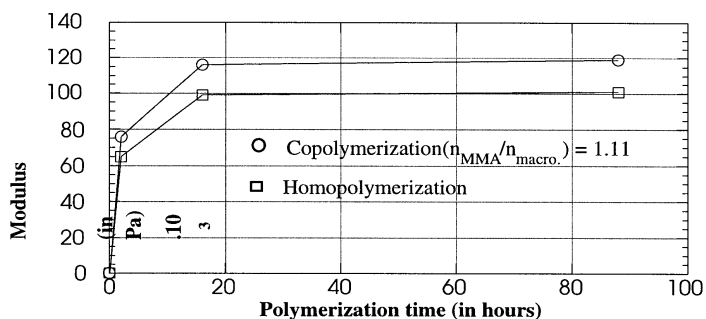


Figure 2. Compression modulus versus polymerization time. Homopolymerization and copolymerization carried out in water.

The presence of MMA tended effectively to accelerate the reticulation process. As indicated in table 1, when higher concentrations of MMA are introduced, the uniaxial compression modulus decreases again. These results must be confirmed by further studies.

Table 2. Physico-chemical characteristics of PEO gels obtained by homopolymerization or copolymerization with MMA in water

r	reaction time (h)	Ceff	ϵ w. % (W)	Qv water (W)	σ (Pa), W
homo	2	0.11	10	9.1	65 000
homo	16	0.14	7.0	7.9	99 000
homo	88	0.14	6.0	7.6	101 000
1.11	2	0.13	8	8.1	76 000
1.11	16	0.15	6.0	6.6	116 000
1.11	88	0.16	5	6.4	119 000

Conclusion

The present work has described the synthesis and the properties of hydrogels obtained by homopolymerization and copolymerization of α,ω -dimethacrylic PEO macromonomers with MMA. That reaction was conducted in organic solvent or in water solution. Preliminary results concerning the influence of the preparation solvent on the properties of such networks could be confirmed unambiguously. The possibility to prepare hydrogels or amphiphilic networks by free radical polymerization directly in water solution opens new perspectives in the domain of macromolecular engineering and in the development of materials based on PEO and specially designed for biomedical applications. The formation in water of hydrophobic domains containing high concentration of polymerizable units is the major explanation for the better mechanical properties of networks obtained in water. These observations should now be supported by light scattering methods in order to determine the size of the domains. The existence of a critical micellar concentration has just been demonstrated for these systems.

Further work is now under progress to extend that polymerization process to bifunctional macromonomers exhibiting different chemical natures: 1;3-Polydioxolane (PDXL) networks (11) and PEO hydrogels containing cleavable PDXL chains (12) have been obtained using similar strategies.

Acknowledgments

We thank Dr. Christopher Plummer for his use of the TEM.

References

1. Bailey Jr JF, Koleske JV(1972) Poly(ethylene Oxide) Academic Press, New York
2. Harris JM (1992) Poly(ethylene glycol) chemistry - Biotechnical and Biomedical Applications, Plenum Press
3. Merrill E.W et al. (1992) Polymers in Medicine Biomedical and Pharmaceutical Applications, RM.Ottenbrite, L.E. Chiellini (Eds) Technonic publishing
4. Gnanou Y, Hild G, Rempp P (1987) *Macromolecules* 20: 1662
5. Schmitt B, Alexandre E, Boudjema K, Lutz PJ (1985) *Macromol Symp* 93: 117
6. Rempp P, Lutz P, Masson P, Franta E (1984) *Makromol Chem Suppl* 8: 3
7. Weiss P, Herz J, Rempp P (1977) *Makromol Chem* 141: 145
8. Ito K, Tomi Y (1992) *Macromolecules* 25: 1534
9. Rempp, E. Franta (1984) *Adv Polym Sci* 58: 1
10. Tsukahara Y, Yamashita Y (1990) *Macromolecules* 23: 5201
11. Sahli N, Belbachir M, Franta E, Lutz P (1997) *Proceedings Symposium on Ionic Polymerization (Paris)*
12. Naraghi K, (in preparation)