

Conformational Changes of Hydrogels of Poly(methacrylic acid) Induced by Interaction with Poly(ethylene glycol)

O. E. Philippova, N. S. Karibyants, and S. G. Starodubtzev*

Physics Department, Moscow State University, Moscow 117234, Russia

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ABSTRACT: Conformational transitions of hydrogels of poly(methacrylic acid) induced by complexation with poly(ethylene glycol) were investigated. The degree of swelling of the interpolymer complex depends strongly on the pH of the solution and on the concentration of poly(ethylene glycol). It was shown that the addition of poly(ethylene glycol) results in sharp conformational transitions of neutral poly(methacrylic acid) gels in the collapsed state due to complex formation between the network and the linear polymer. The addition of the excess of poly(ethylene glycol) leads to reentrant swelling of the gel. A phase transition of the complex PMAA gel-PEG in the collapsed state determined by the concentration of low molecular weight acid in the solution was observed.

Introduction

Polymer networks can form complexes with linear macromolecules via hydrogen bonding. The complexation significantly influences the conformational state of the swollen networks.

The formation of intermacromolecular complexes (IMCs) between the linear polymers poly(methacrylic acid) (PMAA) and poly(ethylene glycol) (PEG) was thoroughly investigated.¹ It has been shown that complex formation results in the transition of polymer coils in the globular state. The IMCs are formed by hydrogen bonding between the carboxy groups of PMAA and the ether oxygen atoms of PEG. These IMCs are also stabilized by hydrophobic interactions.

The complexation phenomena in the swollen PMAA networks can be quite different from those in linear polymers due to the elasticity of the network. The conformational changes of the hydrogels of cross-linked PMAA induced by interactions with linear PEG were observed in refs 2-9. The detail analysis of the degree of swelling and of the composition of the complexes formed by PMAA gels and PEG in neutral aqueous medium was performed in refs 7 and 8. In particular, it has been shown that the increase of the chain length of the linear component results in a strong decrease of the effective dissociation constant of the IMC.

The conformational changes of the PMAA network caused by IMC formation can be of pronounced practical interest. Osada has proposed the use of such complexes to control the contraction of the PMAA membrane.²⁻⁶ The complexes of the PMAA network with PEG can be used as carriers of enzymes and drugs for their controlled release.

Experimental Section

PMAA gels were prepared by free-radical copolymerization of methacrylic acid (99.5 mol %) and *N,N'*-methylenebis(acrylamide) (0.5 mol %) in aqueous solution. Ammonium persulfate (4.4×10^{-3} mol/L) and *N,N,N',N'*-tetramethylethylenediamine (TMED) (4.4×10^{-3} mol/L) were respectively the initiator and the accelerator. Gelation was carried out in cylindrical tubes at room temperature for 24 h. The prepared gel was washed in a large amount of distilled water for 3 weeks. Then the gels were placed in HCl solution of appropriate concentration for 24 h. The weight fraction of the polymer in the swollen network was

determined by the formula $\beta = m_{\text{dry}}/m_{\text{sw}}$, where m_{dry} is the mass of the dry gel and m_{sw} is the mass of the swollen gel. The value of β for the PMAA gel swollen in 5×10^{-4} N HCl solution was 0.024. The IMC composition was characterized by the ratio θ of PEG/PMAA repeating units in the gel. The initial ratio of PEG/PMAA repeating units in solution was designated by q .

PEG with molecular weights 300 and 6000 (Loba Chemie, Wien-Fischamend, Austria) was used without preliminary purification.

To study the PMAA-PEG interaction, the gel samples were put in HCl solutions, containing an appropriate amount of PEG (2 mL of the solution per 1 mg of dried PMAA network). The samples were thermostated at 25 °C, until equilibrium was reached (for 3-4 weeks). The relative mass of the sample was characterized by m/m_0 ratio, where m is the mass of the sample at the equilibrium state and m_0 is the mass of the sample after synthesis.

The concentration of PEG in solution was determined by the method described in ref 10. This method is based on spectrophotometric measurement of a complex formed between PEG and barium iodide. Two milliliters of PEG solution was added to 0.5 mL of 5% (w/v) barium chloride in 1 N HCl. To this mixture was added 0.25 mL of a solution prepared by dissolving 1.27 g of iodine in 100 mL of 2% (w/v) potassium iodide. In the present work, the volume of the solution of iodine and potassium iodide was halved in comparison with the procedure described in ref 10. Color was allowed to develop for 15 min at room temperature and the optical density was registered at 535 nm against a reagent blank prepared as above but substituting water for the sample. Measurements were made using a LKB Ultrospec 4050 UV/visible spectrophotometer. For IMC formed in PEG solutions of initial concentrations less than 0.26 wt %, the PEG content in the IMC was calculated by subtraction of the equilibrium concentration of PEG in the surrounding solution from the initial concentration of PEG.

To determine the composition of IMC formed in the PEG solutions of initial concentrations higher than 11 wt %, the gel samples were extracted from solutions and dried to constant mass. Then the mass of PEG in the IMC was calculated by subtraction of the initial mass of the dried network from the total mass of the dried residue.

The infrared spectra were recorded with a Bruker IFS-45 Fourier transform infrared spectrometer (Bruker Analytische Messtechnik GMBH, Rheinstetten, Germany) at a resolution of 2 cm^{-1} . A minimum 32 scans were signal averaged. The samples of dried gels were examined as pressed KBr disks.

Results and Discussion

In the previous study,⁸ it has been shown that when the hydrogel of PMAA is put in an aqueous solution of PEG, the linear polymer penetrates into the network. The content of PEG in the gel phase increases with time and

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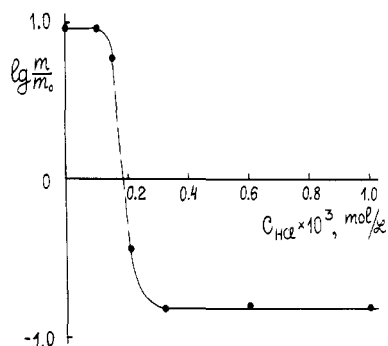


Figure 1. Dependence of the relative mass of the PMAA gel-PEG 6000 complex on the concentration of HCl in aqueous solution at a PEG/PMAA initial ratio $q = 5.0$.

reaches its limiting value. The absorption of PEG leads to the contraction of the gel. The relative mass of the gel is lowered by a factor of 1.5–3.0. The FTIR spectroscopic data indicate that the slight deswelling of PMAA gel is accompanied by the complex formation between PMAA gel and PEG. It was also found⁸ that the addition of a small amount of a strong acid (HCl) in the solution containing IMC equilibrated with PEG leads to the 30-fold decrease of the gel volume. One can suppose that there is a phase transition of the complex in the collapsed state determined by the concentration of the acid in the solution.

This assumption is supported experimentally. Figure 1 illustrates the dependence of the relative mass of the PMAA gel-PEG 6000 complex on the concentration of HCl in aqueous solution. The initial ratio PEG/PMAA of repeating units q in the system amounted to 5.0. It can be seen that up to a concentration of the acid of 1.5×10^{-4} mol/L, the gel is in a highly swollen state. A further increase of the concentration up to 2.0×10^{-4} mol/L results in the jumpwise transition of the gel in the collapsed state. Thus, a small change of pH induces a drastic jumplike conformational transition accompanied by a 30-fold shrinking of the network.

It is to be noted that there are two possible reasons for the contraction of the gel in the solution of the linear polymer: (1) the osmotic deswelling of the gel in the polymer solution (no complex formation); (2) the complex formation between the network chains and the linear polymer.

To discriminate between these two cases, there is a need to examine the IMC formation in the gel. As was mentioned above, in our previous work it was shown⁸ that the slight deswelling of PMAA gel in the absence of HCl is accompanied by the complex formation between PMAA gel and PEG. Thus, even in the absence of HCl the main reason for the contraction of the gel is the IMC formation.

As pointed out above, the complex formation between linear PMAA and PEG results in the transition of polymer coils in the globular state. The linear PMAA-PEG complex does not dissolve in water, but it is soluble in aqueous-organic solvent mixtures.¹¹ The hydrophobic nature of linear PMAA-PEG complexes is manifested also in the aggregation of such IMCs with each other in aqueous media. At elevated temperatures, the aggregation of complexes is accelerated. In comparison with polyelectrolyte complexes, the rate of aggregation of hydrogen-bonded complexes is much faster. From these results, it was suggested¹ that the driving forces of the aggregation of the complex are partly hydrophobic interactions.

The contraction of PMAA gel in the presence of PEG is probably due to the formation of hydrophobic IMCs via hydrogen bonds between PMAA and PEG. But a small

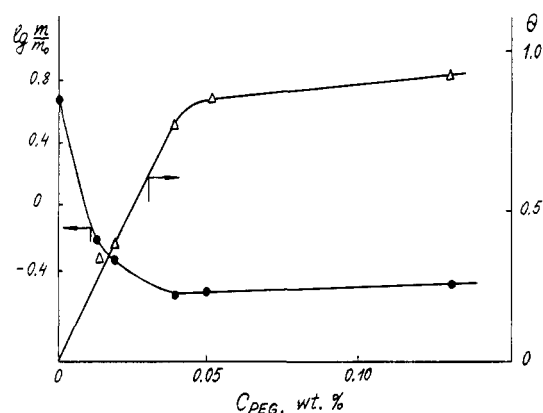


Figure 2. Dependence of the relative mass and composition θ of the PMAA gel-PEG 6000 complex on the initial concentration C_{PEG} of PEG in a 5×10^{-4} mol/L solution of HCl.

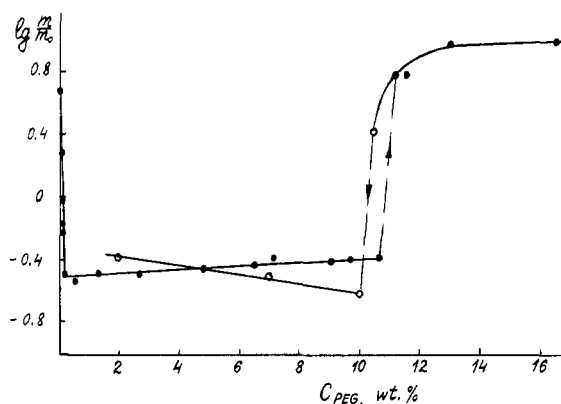


Figure 3. Dependence of the relative mass of the PMAA gel-PEG 6000 complex on the initial concentration C_{PEG} of PEG in a 5×10^{-4} mol/L solution of HCl. Filled circles denote the curve on raising the concentration of PEG in solution. Open circles are for the curve on lowering the concentration of PEG in solution.

amount of H^+ ions arising from the dissociation of COOH groups of PMAA produces excessive osmotic pressure in the swollen network, which prevents the collapse of the gel. In the solution of the acid, the dissociation of PMAA is suppressed. This leads to the lowering of the osmotic pressure in the swollen network and to the collapse of the gel. It should be noted that the fraction of HCl which causes the transition is very small and amounts to only 0.8% with respect to the total number of PMAA repeating units.

In further experiments, we have studied the influence of the concentration of PEG on the conformational state of PMAA gel. In order to suppress the dissociation of PMAA, these experiments were performed in acidic medium (in 5×10^{-4} mol/L HCl). Figures 2 and 3 illustrate the dependence of the relative mass of the gel on the initial concentration of PEG 6000 in the solution (C_{PEG}). The obtained results show that the addition of a small amount of PEG in the solution leads to the contraction of the PMAA gel. In this region, the concentration of PEG in the IMC increases with the initial concentration of PEG in solution (Figure 2). It is seen that the addition of only 0.05 wt % PEG results in the collapse of the PMAA gel. The minimum value of the relative mass of the gel is attained at the initial PEG/PMAA ratio in repeating units (q) equal to 2. In these conditions, the PEG/PMAA ratio (θ) in the IMC amounts to approximately 1.0. As discussed above, the formation of hydrophobic IMC is responsible for the collapse of the gel.

Then, in the large region of PEG concentration (0.05–10.8 wt %), the relative mass of the gel changes insignif-

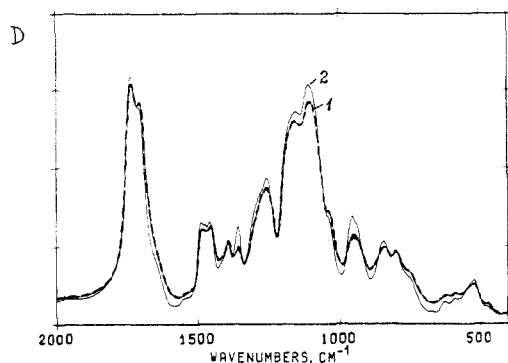


Figure 4. IR spectra of the PMAA gel-PEG 6000 complexes formed in 0.13 wt % (1) and 7.9 wt % (2) solutions of PEG in a 5×10^{-4} mol/L HCl.

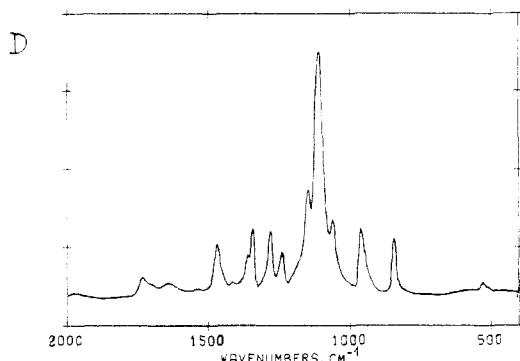


Figure 5. IR spectrum of the PMAA gel-PEG 6000 complex formed in a 13.0 wt % solution of PEG in a 5×10^{-4} mol/L HCl.

icantly (Figure 3). The PEG/PMAA ratio in the IMC remains almost constant ($\theta = 1$). Figure 4 illustrates that the IMCs formed in the solution of PEG of various initial concentrations (0.13 and 7.9 wt %) have similar IR spectra. It should be noted that in these spectra there are two bands in the region of C=O stretching vibrations: (1) at 1700 cm^{-1} , corresponding to dimeric carboxy groups; (2) at 1730 cm^{-1} , which can be assigned to carboxy groups in H complexes with the ether oxygens of PEG. The analogous two absorption bands are presented in the IR spectra of the linear atactic PMAA-PEG complexes.^{12,13} Therefore, even at the significant excess of PEG ($q = 2-440$), a part of the COOH groups of PMAA gel does not form a complex with the ether oxygens.

A further increase of the PEG concentration results in a very sharp transition of the gel in the highly swollen state. In the interval of concentrations of PEG between 10.8 and 11.1%, the relative mass of the gel increases by a factor of 15. A drastic increase in the relative mass of the gel is attended with the sharp rise in content of PEG in the gel. The IR spectrum of the gel equilibrated in a 13.0 wt % solution of PEG is presented in Figure 5. From this spectrum, we notice that the dried residue of the gel phase consists almost entirely of PEG and the fraction of PMAA in the gel is very small. The value of θ for this sample amounted to 50. It should be pointed out that in this case the concentration of PEG in the gel phase (17.2 wt %) is only slightly higher than the concentration in the surrounding solution (12.4 wt %).

When the concentration of PEG 6000 in solution was lowered starting from 11.1 wt %, the gel shrinks discontinuously to 25 times its volume at C_{PEG} of approximately 10.0 wt %. The transition concentrations upon raising and lowering C_{PEG} are different by approximately 1 wt %. The analogous hysteresis was observed in ref 14 in equilibrium swelling curves of copolymer gels of *N*-isopropylacrylamide and bis[4-(dimethylamino)phenyl](4-

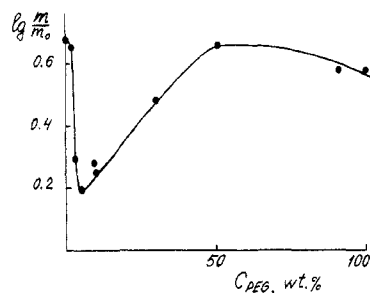


Figure 6. Dependence of the relative mass of the PMAA gel-PEG 300 complex on the initial concentration of PEG in a 5×10^{-4} mol/L solution of HCl.

vinylphenyl)methyl leucocyanide under ultraviolet irradiation when the temperature was changed.

At a further increase of the initial concentration of PEG from 11.1 to 17.0 wt %, the relative mass of the gel remains constant (Figure 3). The PEG/PMAA ratio in the gel under these conditions changes insignificantly. The values of θ are equal to 50 and 53 for the gel samples equilibrated in 13.0 and 17.0 wt % solutions of PEG, respectively.

Thus, at a definite concentration of solution of PEG, a jumplike penetration of PEG macromolecules in the collapsed gel is observed. This effect results in the decollapse of the gel. One can suppose that energetic interactions of PEG macromolecules with the IMC are more favorable than with solvent. But the penetration of additional PEG molecules in the collapsed gel leads to a significant loss of entropy. The concentration of linear polymer outside the network increases. Then, in a narrow region of PEG concentration, the excess linear polymer penetrates into the network, which induces the reswelling of the gel. The reason is the gain in energy caused by contacts between the IMC and linear polymer. The possibility of reentrant swelling transition of the gel in concentrated solutions of linear polymer was predicted theoretically in ref 15.

The thermodynamic theory of swelling and collapse of networks in the solution of linear polymers capable of forming complexes with the network chains was developed by Khokhlov and Kramarenko.¹⁵ The theory indicated that the character of the behavior of the network depends on the degree of polymerization of linear polymer. The theoretical consideration results are presented in ref 15 for linear polymers with degrees of polymerization p amounting to 10 and 100. The main distinction is that the swelling of the network at high concentrations of linear polymer is realized as a first-order phase transition with a jump of the network volume and of the fraction of linear polymer inside the network in the case of linear polymer with $p = 100$. Besides, the magnitude of the collapse of the network, which interacts with polymer with $p = 100$, is larger.

Really, these theoretical calculations were confirmed by our experimental data. Figure 6 illustrates the dependence of the relative mass of the PMAA gel on the initial concentration of PEG 300 in 5×10^{-4} mol/L solution of HCl. It can be seen that the addition of PEG in the solution leads to the contraction of the gel. The relative mass of the gel decreases by a factor of 3, and in the presence of PEG 6000 under the same conditions, it decreases by a factor of 17. Thus, by the convenience of theory, the collapse of the network is more pronounced as a result of complexation with PEG of higher molecular mass.

It is known that the stability of IMCs between linear PMAA and PEG lowers sharply with the decrease of the length of PEG macromolecules.¹⁶ PEG of molecular mass

lower than 1000 does not form a complex with linear PMAA at room temperature.¹⁶ Hence, it was necessary to determine whether low molecular weight PEG penetrates into the network. The IR spectroscopic data indicate that the contraction of PMAA gel in the solution of PEG 300 is accompanied by a penetration of PEG molecules into the network.

When the minimum value of the relative mass of the gel is attained, a further increase of the concentration of PEG 300 results in the swelling of the gel. The network does not remain in the collapsed state as in the case of PEG 6000. The reswelling of the gel is observed in a large region of C_{PEG} . For PEG 6000, this transition is realized in a jump-like fashion.

At higher concentrations of PEG 300, the dimensions of the gel slightly decrease with the rise of C_{PEG} (Figure 6). This effect was not observed for PEG 6000 because of the relatively small range of C_{PEG} in the experiment. A slight decrease of the relative mass of the gel can be explained by the well-known effect of screening of excluded volume interactions in concentrated polymer solutions.¹⁵

Therefore, the experimental data obtained are in good agreement with theory.

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