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Synthesis of new thermosensitive copolymers based on 2-hydroxyethylacrylate and 2-hydroxyethylmethacrylate and their interaction with surfactants

Abstract

Thermo-sensitive linear and cross-linked copolymers based on 2-hydroxyethylacrylate and 2-hydroxyethylmethacrylate were synthesized and their physicochemical properties were investigated. It was found that copolymer solutions have LKST and copolymer hydrogels of certain composition undergoes sharp collapse at temperature increase. The interaction of copolymers with surfactants was studied. It was shown that swelling behavior of copolymers in surfactants aqueous solutions depend on several factors: copolymer composition, surfactant concentration. The reason for the observed phenomenon is discussed. Treatment of some hydrogels in surfactant solutions resulted in great enhancing of collapse amplitude and its sharpening.

Keywords: Thermo-sensitive copolymers, 2-hydroxyethylacrylate and 2-hydroxyethylmethacrylate.

Introduction

Some amphiphilic polymers are able to self-association in aqueous solutions and undergo reversible phase transition. Many transitions are based on a change of hydrophilic qualities of certain moieties, some transition reported such as pH – or light induced and other phase transitions are based on physical interactions between their hydrophobic moieties. The nature of hydrophobic interaction has not been fully clarified yet. However its existence is accepted and is widely used for explanation of physicochemical behavior of polymers. Some phase transitions induced by increased hydrophobic interactions at changed conditions are in molecular scale a coil-globule conformational change. Further their increase is followed by organization of single globule macromolecules into micelle-like structures. Then those may gradually interact with each other. At that in a lower concentration range generally a precipitation occurs, and at higher concentrations those primary structures aggregate and interconnect into network-like structure [1]. For cross-linked swollen polymers the phenomena is expressed in a volume phase transition. In other words, when polymer-polymer interactions

become preferable instead of polymer-solvent interactions, macromolecules accept convolute globule conformation and hydrogel sample collapses decreasing its volume in dozens of times, and solvent exclusion takes place [2].

Among all stimuli-sensitive polymers, those demonstrating temperature dependent behavior attract a great attention from both fundamental and practical points of view. In particular, thermo-sensitive polymers may find widespread application as sensors, actuators, controlled and targeted drug delivery systems [3], non-viral vectors for gene therapy [4], attachment /detachment of cultured cells [5], etc.

Modification of existing thermo-sensitive polymers in order to vary conditions of the phase transition along with pure synthetic methods can be carried out by complexation with ionic surfactants through hydrophobic interaction. Normally it results in conversion of the polymer into ionic onece that enhances the polymer solubility in aqueous environment and this effect is more impressive with higher surfactant concentrations [2,6]. Efficiency of interaction between non-ionic polymer and ionic surfactant depends on hydrophobicity of polymer as well as on both structure and hydrophobicity of the surfactant [6,7].

Safrany A. synthesized hydrogels based on 2-hydroxyethylacrylate (HEA) and 2-

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hydroxyethylpropylacrylate (HPA) by free radical γ -induced copolymerization. Due to the presence of both hydrophilic (HEA) and hydrophobic (HPA) units, those copolymers exhibited thermo-induced collapse behavior in water solutions [8]. But pure HEA hydrogels swell at all temperatures up to 70°C and pure HPA hydrogels collapse above 16°C, therefore inverse thermo-response of HEA-HPA copolymers was predictable. In general, a copolymerization of hydrophilic and hydrophobic comonomers is a common method to obtain highly swollen hydrogels contracting at increasing of the temperature. We have synthesized thermo-sensitive HEA-HEMA copolymers of linear and cross-linked structure by free radical copolymerization. The interactions of thermo-sensitive hydrogels with ionic surfactants can be used as very promising method for improving of its stimuli-sensitive properties. In this paper we have attempted to modify thermo-sensitive properties of non-ionic amphiphilic copolymers based on 2-hydroxyethylacrylate and 2-hydroxyethylacrylate through interactions with ionic surfactant.

Materials and Methods

Materials

Commercial 2-hydroxyethylacrylate (HEA), 2-hydroxyethylmethacrylate (HEMA) (96% wt. purity), crosslinker poly(ethylene glycol dimethyl acrylate) (PEGDMA), 2,2-azobis(isobutyronitrile) (AIBN) were purchased from Aldrich Chemical Co. HEA and HEMA were purified by vacuum distillation (<1 Pa) under argon atmosphere. AIBN was double recrystallized from ethanol ($T_{\text{melting}}=374$ K). Surfactants sodium dodecyl sulfate (SDS) and cetyl pyridinium bromide (CPB) (99% wt. purity) were purchased from Altey Co. and were used as received. The structures of HEA, HEMA, SDS and CPB are shown in Fig. 1.

Copolymerization

HEA-HEMA copolymers of linear and cross-linked structure were synthesized by free radical copolymerization (90% vol. of solvent). The copolymerization was carried out in the sealed glass ampoules at $T = 60$ °C. The aqua solution of ethanol (50% v/v) was used as solvent. Before synthesis the feed mixture was saturated by argon. Concentration of cross-linking agent and

initiator were 0.5% vol. and 1% wt., respectively. The linear copolymers were double precipitated from ethanol into acetone. Then they were dried under vacuum and stored at $T = -5$ °C. Copolymer hydrogels were washed in water for several days to remove the unreacted monomers and linear polymers.

Copolymer characterization

The compositions of the copolymers were determined by elemental analysis (PERKIN 85 ELMER Series II CHNS/O Analyzer 2400), IR-spectroscopy (FTIR Satellite "Mattson", USA) and ^1H and ^{13}C NMR-spectroscopy (Bruker ARX300 spectrometer at 300 and 75 MHz, respectively). Molecular-weight characteristics were obtained using gel-permeation chromatograph, equipped by Aligent 1100 series RI detector, quaternary pump and WATER Ultrahydrogel columns.

LCST diagram was obtained as follows. Aqueous polymer solutions (0.01-12% w/v) were poured into glass tubes and sealed. Cloud points were determined visually in a water bath taken at a temperature when any noticeable turbidity appeared. The rate of temperature changes in the water bath was 1 °C/30 min. Phase diagrams 'cloud point-polymer solution concentration' were constructed and the lower critical solution temperature (LCST) was determined. The viscosity of copolymers solutions was measured in an Ubbelohde viscometer at 20 ± 0.1 °C. The swelling ratio was calculated from V/V_0 , where V is the volume of the gel at ambient conditions, and V_0 is its volume at the synthesis. Value of the volume of hydrogel samples was obtained using cathetometer B-320. Temperature dependent measurements were carried out in a thermostated water bath.

Thermo-induced phase transition

Thermo-induced collapse was studied in water in term of swelling ratio V/V_0 of the hydrogels as a function of temperature. The temperature was gradually increased with step about 3-5 degrees, and the hydrogels were allowed to adjust conditions for 30 min at each experimental point prior measurement.

Hydrogel – surfactant interaction

After synthesis the hydrogel samples were kept in distilled water prior to interaction with

surfactants. Disk-shaped samples of about 0.50 ± 0.02 g weights were then immersed into a surfactant solution (20 ml) of certain concentrations and the kinetics of volume changes was controlled. The sorption of the CPB by the hydrogels was observed by spectrophotometric method at a wavelength of 260 nm (UV-VIS spectrophotometer Shimadzu, Japan) under isothermal condition (25°C). Extinction coefficient ϵ_{260} was $3850 \text{ L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$.

As the parameters of V/V_0 and incident intensity quit changing, the interaction was considered reaching equilibrium. After that the hydrogels were washed from excess of surfactant molecules on their surface and in bulk by replacement into glass of water at room temperature, and swelling ratio was measured with time.

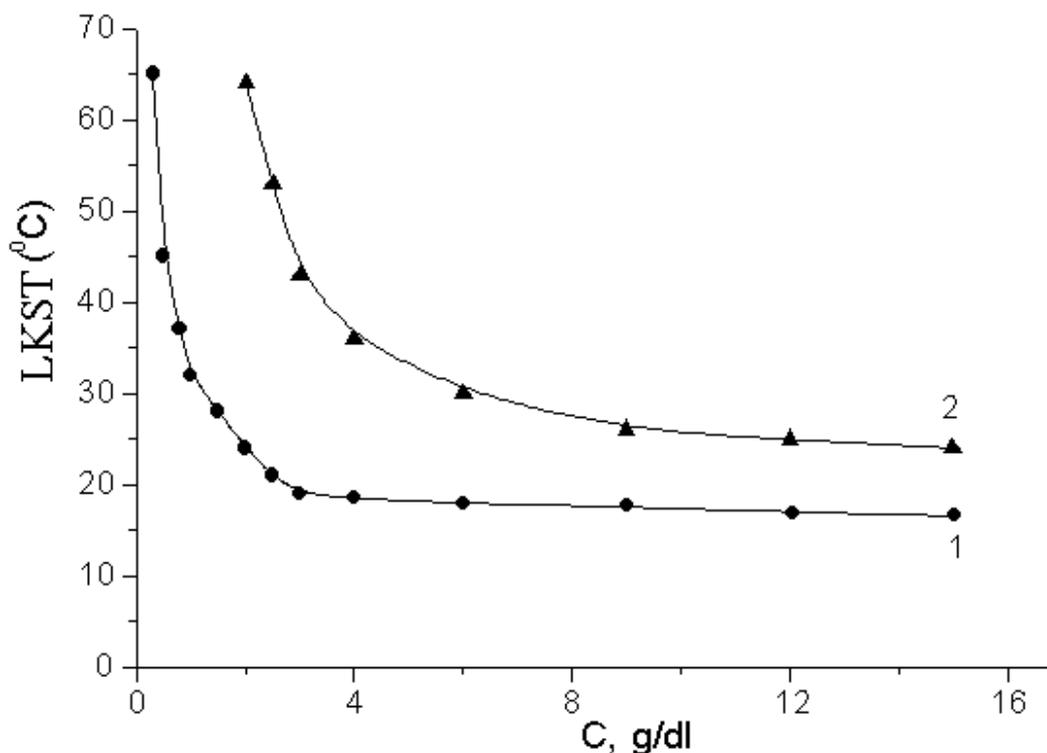
Results and Discussion

Copolymers synthesis and characterization

We used PEGDMA instead of EGDMA as cross-linker to enhance swelling degree of HEA-HEMA hydrogels. Also we have chosen

copolymerization in the ethanol:water (50:50 v/v) mixture instead of the copolymerization in bulk for the same reason. It is found that HEA and HEMA differ in the structure just for one methyl group but this negligible change in the structure results in appearance of LCST of aqueous solutions of HEA-HEMA copolymers (Fig. 1). The LCST appearance we observed was expected because both HEA and HEMA homopolymers are hydrophilic and aqueous solutions of these homopolymers don't show LCST.

Composition (obtained by NMR-spectroscopy) and molecular-weight characteristics (obtained by gel permeation chromatography) of the synthesized HEA-HEMA copolymers are shown in table 1. It is shown, that content of monomers in copolymer is the same as content of monomers in initial monomer mixture. Evidently, it is related to the same activity of HEA and HEMA in copolymerization reaction. One can see, that equilibrium swelling degree, α , of HEA-HEMA hydrogels reduces with increasing of the content of HEMA. It can be explained by increasing of content of hydrophobic methyl groups of HEMA in copolymer structure.



[HEA]:[HEMA], mol%: 1 – 91.3:8.7; 2 – 81.5:18.5.

Figure 1 - Dependence of LCST of HEA-HEMA copolymers on the temperature in aqueous solutions.

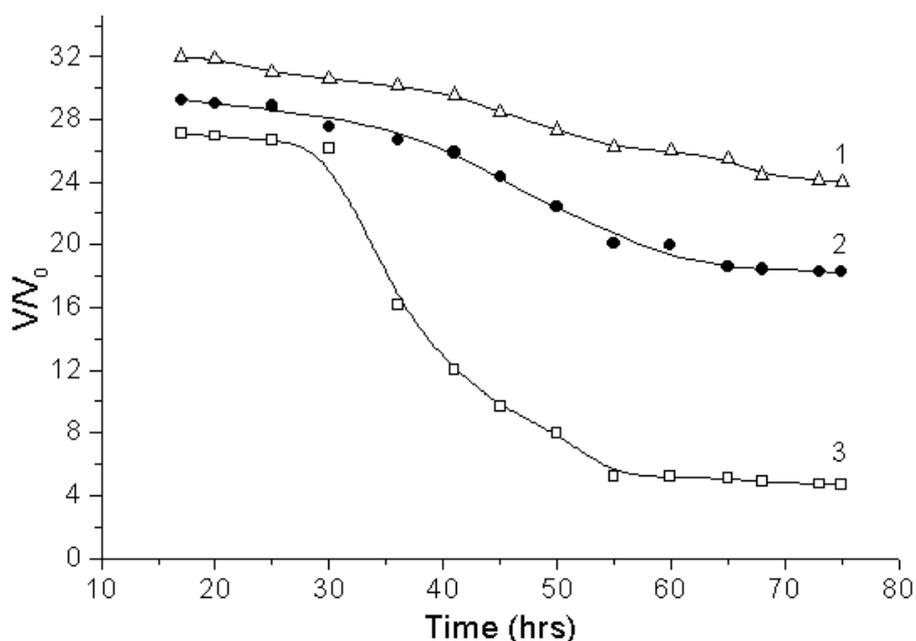
Table 1 –Characteristics of HEA-HEMA copolymers

[HEA]:[HEMA], mol% in initial monomer mixture	[HEA]:[HEMA], mol% in copolymer	M_n	M_w	Polydis- persion degree	α , g/g equilibrium swelling degree
90:10	91.3:8.7	$1,67 \times 10^6$	$2,79 \times 10^6$	1,66	34
[HEA]:[HEMA], mol% in initial monomer mixture	[HEA]:[HEMA], mol% in copolymer	M_n	M_w	Polydis- persion degree	α , g/g equilibrium swelling degree
80:20	81.5:18.5	$2,73 \times 10^6$	$3,14 \times 10^6$	1,15	32
70:30	71.7:28.3	$2,75 \times 10^6$	$3,08 \times 10^6$	1,12	28
60:40	60.8:39.2	$2,95 \times 10^6$	$3,30 \times 10^6$	1,12	-
50:50	50.2:49.8	$3,23 \times 10^6$	$3,54 \times 10^6$	1,09	-

Apparently, LCST of HEA-HEMA copolymers is caused by appearance of hydrophobic methyl groups of HEMA in copolymer structure. As shown in Fig. 1, linear HEA-HEMA copolymers have LCST in the range 17-65 °C, depending on the monomer ratio: the higher the ratio of more hydrophobic HEMA, the lower the LCST.

The data obtained for linear copolymers correlate with data obtained for copolymer hydrogels. For those synthesized in this work, the swelling behavior upon the temperature presented in Fig. 2. As it is seen, all samples undergo contraction with increasing temperature. For samples 1 and 2 (Fig. 2, curves 1, 2) that are more

hydrophilic, contraction occurs not expressively. Hydrophobic interaction in their macromolecules is not strong enough due to a low content of hydrophobic methyl groups. So that higher temperature is required to turn the macromolecules to collapsed state. The difference in swelling ratio at the lowest and the highest temperatures in studied range for these samples that we call here as amplitude of contraction, is significantly less than that for the sample 3 (Fig. 2, curve 3). It is characterized by the highest content of hydrophobic units. That is why it exhibits an expressive contraction with high amplitude upon the temperature increase.



mol%: 1 – 91.3:8.7; 2 – 81.5:18.5; 3 – 71.7:28.3.

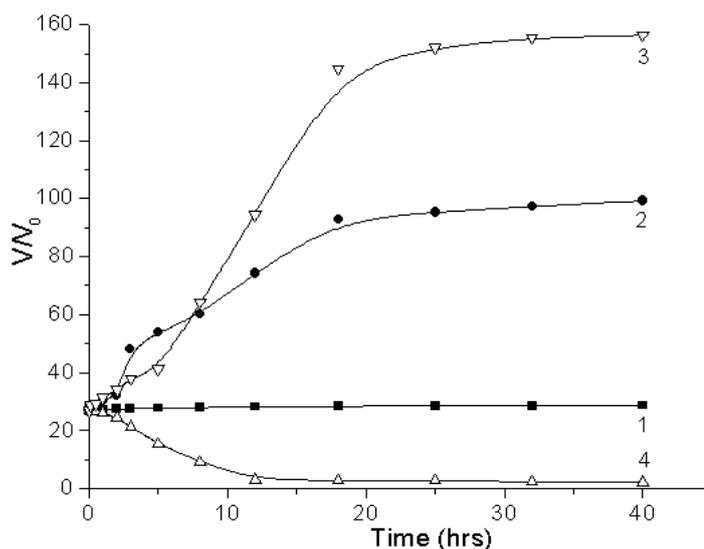
Figure 2 – Dependence of swelling ratio of HEA-HEMA hydrogels on the temperature in aqueous solutions. [HEA]:[HEMA].,

Interaction of copolymers with surfactants

Thus, for a hydrogel to show impressive thermo-collapse, it should swell significantly in water and simultaneously have sufficiently high content of hydrophobic groups along its polymer backbone to provide strong hydrophobic interaction. As mentioned in the introduction, an interaction of non-ionic polymers contained hydrophobic moieties with ionic surfactants is a very effective method to increase solubility of the polymers due to electrostatic repulsion between likely charged surfactant's heads attached along the polymer backbone, while concentration of hydrophobic groups in copolymer composition remains to be high. Here this method was used to improve stimuli-sensitive properties of HEA-HEMA copolymers. Cationic cetyl pyridinium bromide (CPB) and anionic sodium dodecyl sulfate (SDS) were used as surfactants.

For investigation of interaction between HEA-HEMA hydrogels and surfactants, samples in equilibrium-swollen state were transferred from water into CPB and SDS solutions at fixed temperature of 20°C. Their swelling behavior was observed in course of interaction through measurement of their swelling ratio V/V_0 (Fig. 3). HEA-HEMA hydrogels either swell or contract depending on surfactants concentration: if concentration of surfactants is sufficiently high (Fig. 3, curves 2, 3) then hydrogels swell else hydrogels contract (Fig. 3, curve 4). Because the mechanism of surfactant binding onto

hydrophobically (if we will consider that HEMA is a hydrophobic comonomer) modified hydrogels is unknown and the complexity introduced by multiple interaction parameters (polymer-polymer; polymer-water; polymer-surfactant; water-water; water-surfactant; and surfactant-surfactant) in these multicomponent systems, the explanation for such behavior is at present tentative. We can note firstly that the hydrogels do not contain ionizable groups in their chemical structure; hence, they should not be any electrostatic repulsion forces between the polymer chains. The observed effects of the ionic surfactants SDS and CPB on HEA-HEMA hydrogels can thus be readily understood by assuming that the gel is ionized upon binding of surfactant molecules to the polymer network. It is reasonable to suppose that the SDS binds to the polymer network within the gel phase through hydrophobic interactions. The SDS and CPB molecules consist of a long aliphatic hydrocarbon chain and HEA-HEMA copolymers have hydrophobic methyl moieties as side groups. When SDS and CPB molecules diffuse into the gel network of copolymer, association should take place through the hydrophobic interaction between the methyl groups of hydrophobic comonomer and long chain alkyl groups of surfactants, thus increasing the surface charge density of hydrogels as the neutral polymers chains become polyelectrolytes.



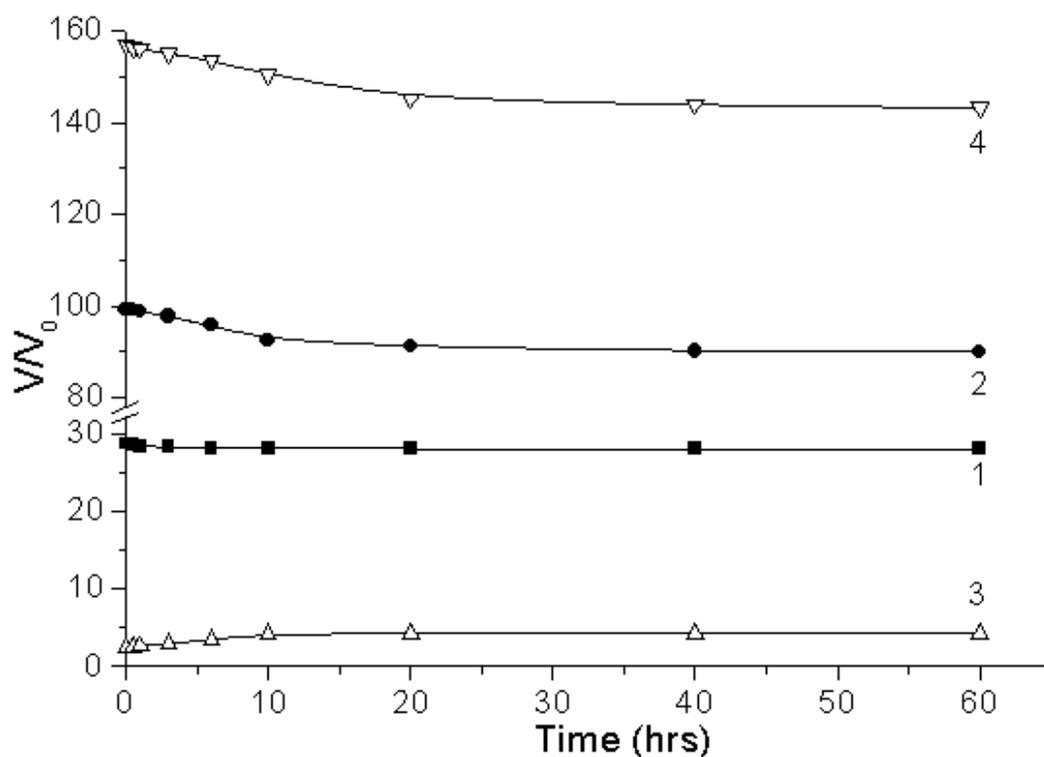
T = 20°C, [HEA]:[HEMA] = 71.7:28.3 mol%, in [SDS], 10^{-3} mol/L: 1 (sample V1) – 5; 2 (sample V2) – 16; in [CPB], 10^{-4} mol/L: 3 (sample V3) – 1; 4 (sample V4) – 10.

Figure 3 - Kinetics of swelling ratio changes of HEA-HEMA hydrogels in differently concentrated surfactant solutions.

These acquired network charges and the counterions associated to the charges exert an extra osmotic pressure on the network. As a result, the polymer conformation will become more like an expanded coil than a globule, and hydrogels swell. On the other hand at low concentration of surfactant such interaction leads to formation of additional junctions. It is caused by surfactant micelles formed in the hydrogel act as additional cross-linking aggregates, resulting in contraction of hydrogel. Swelling behavior of copolymer hydrogels in surfactant solutions can be explained by dominance of the one of two factors above mentioned.

The kinetics of the surfactant sorption by HEA-HEMA hydrogels of different composition was studied and data are shown in Fig. 4. The amount of the surfactant absorbed by the hydrogels was calculated from data of UV-spectrophotometry. Amount of the surfactant, n ,

absorbed by the network was calculated in respect 1 mol of surfactant to 1 mol of dry gel. The lowest value of n is found for the sample 1 (Fig. 4, curve 1), the most hydrophilic hydrogel of HEA-HEMA. The sample 2 (Fig. 4, curve 2) absorbs almost 2 times higher and sample 3 (Fig. 4, curve 3) almost 3 times higher amount of the surfactant in comparison with sample 1. Evidently, that it is connected with increasing of HEMA content: the more hydrophobic comonomer content the more surfactant sorption. It is also point out the hydrophobic nature of polymer-surfactant interaction. It should be noted, that very negligible amount of CPB absorbed by HEA-HEMA hydrogels from diluted aqueous surfactant solutions induced significant changes in their swelling ratio.



T = 20°C, 1 – sample V1; 2 – sample V2; 3 – sample V3; 4 – sample V4 (sample characteristics see in Fig. 3).

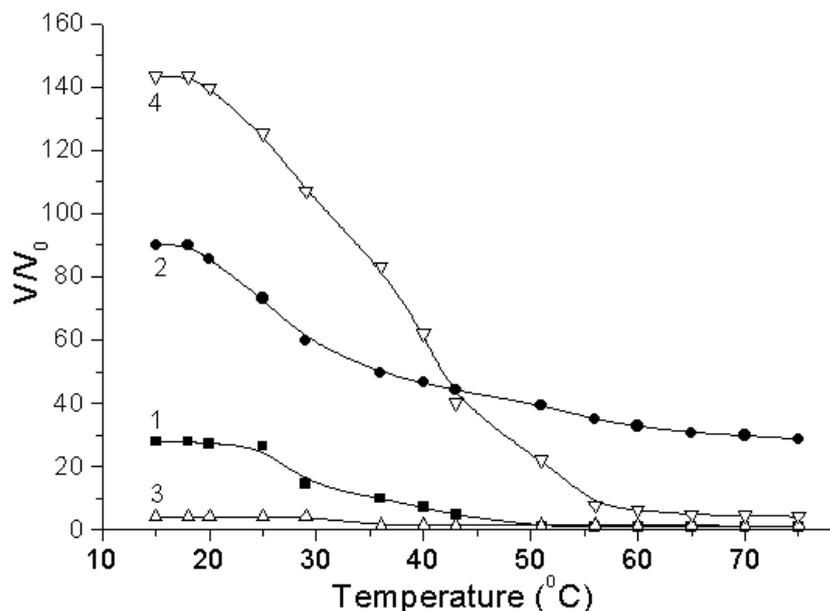
Figure 4 - Kinetics of swelling ratio changes of HEA-HEMA-surfactant complexes after interaction with surfactants solutions.

As equilibrium state was achieved, the networks were removed from surfactant solutions and transferred into distilled water. That resulted in negligible changes of swelling ratio of the hydrogels (Fig. 5). Probably, it may indicate partial destroying of the complex and release of

some part of the surfactant molecules that results in changes. However most of them remain within the network as far as the hydrogels remain swollen (Fig. 5, curves 2, 4) or collapsed (Fig. 5, curve 3) much higher than parent ones. Another reason could be the deterioration of solvent

thermodynamic quality occurs at transfer from surfactant solution to water for amphiphilic

hydrogels, especially for ones with high hydrophobic component content.

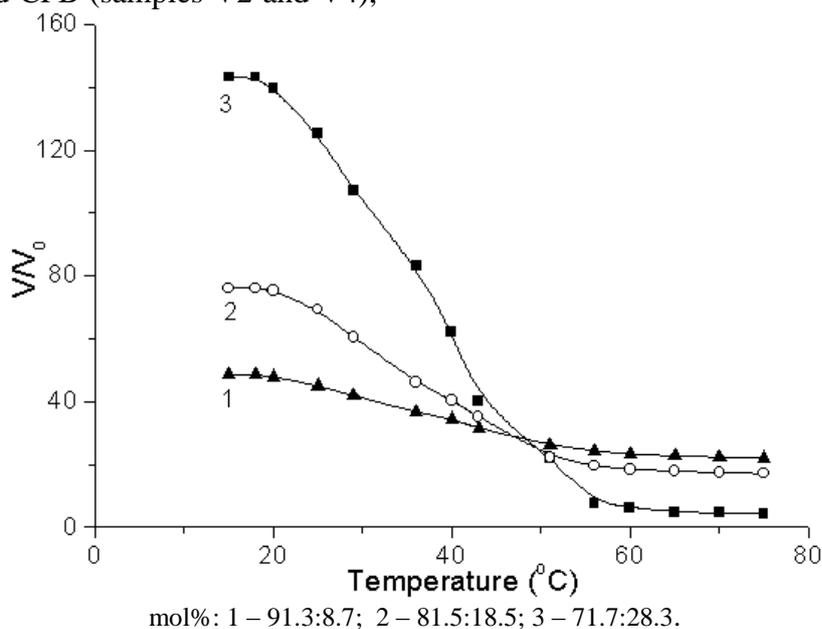


1 – sample V1; 2 – sample V2; 3 – sample V3; 4 – sample V4 (sample characteristics see in Fig. 3).

Figure 5 - Dependence of swelling ratio of HEA-HEMA-surfactant complexes on the temperature in aqueous solutions.

The HEA-HEMA hydrogel-surfactant polycomplexes were studied from their thermo-sensitive properties point of view in terms of swelling ratio versus temperature (Fig. 6). As seen from this figure, the hydrogels contract significantly upon the temperature increase. For polycomplexes, obtained by interaction of hydrogels with high concentrated aqueous solutions of SDS and CPB (samples V2 and V4),

amplitude of contraction is great. As seen from Fig. 6, for slightly hydrophobic sample (Fig. 6, curve 1) the contraction is not expressed, while the sample with the highest content of hydrophobic component (Fig. 6, curve 3) undergoes strongly pronounced collapse with extremely high amplitude, what was not observed for the parent hydrogels of any composition.



mol%: 1 – 91.3:8.7; 2 – 81.5:18.5; 3 – 71.7:28.3.

Figure 6 – Dependence of swelling ratio of HEA-HEMA-CPB complexes on the temperature in aqueous solutions. Content of HEA-HEMA copolymers used: [HEA]:[HEMA].

The greatest value of swelling ratio that we could achieve for HEA-HEMA hydrogels in our laboratory varying synthesis conditions in wide range, was 32, whereas hydrogels modified with CPB demonstrate value of V/V_0 at room temperature close to 156. Except for noticeable increase of amplitude and narrowed temperature interval of collapse, a certain shift in temperature interval of collapse to a higher range should be noted.

Obviously, the presence of ionic heads of the surfactant increases the network hydrophilicity while the presence of hydrophobic tails of the surfactant helps contraction of the modified network.

Conclusion

HEA-HEMA copolymers were prepared by free radical copolymerization and their physicochemical properties were investigated by NMR-, spectroscopy, gel permeation technique. The interaction of copolymers with surfactants was studied. It was observed that thermo-sensitive properties of HEA-HEMA hydrogels modified by complexing with cationic CPB and anionic SDS, are greatly improved, and hydrogels treated by surfactant solutions undergo sharp thermo-induced collapse with high amplitude.

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