International Journal of Biology and Chemistry 11, № 1, 153 (2018)

IRSTI 31.25.19

A.N. Azhkeyeva, R.K. Rakhmetullayeva, G.Zh. Yeligbayeva,
Ye.M. Shaikhutdynov, U. Nakan, M. Abutalip, K. Park

Institute of chemical and biological technologies, Satbayev Univesity, Almaty, Kazakhstan
*e-mail: ayganym_90@mail.ru

Synthesis of novel thermosensitive copolymers based on ethylacrylate

Abstract. New thermo-sensitive copolymers (CPL) based on 2-hydroxyethylacrylate (HEA) and ethylacrylate (EA) were synthesized by radical copolymerization method. The composition of CPL, copolymerization activity were calculated. Physicochemical properties of new water-soluble CPL with composition of initial monomer mixture 90:10%; 80:20%; 70:30; 60:40%; 30:70%; 20:80%; 10:90% were investigated. The main regularities of the thermo-sensitive behavior of CPL were studied.

We found the compositions of copolymers and calculated the relative activities of comonomers the values of which evidence the higher reactivity of ethylacrylate compared with the reactivity of hydroxyethylacrylate. The study of phase diagrams of aqueous solutions of copolymers allowed identifying the presence of lower critical solution temperature (LCST).

As the main physicochemical methods of investigation, in work are used: IR-, ^{1}H NMR-, UV- spectroscopy, thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), turbidimetry.

Key words: Radical copolymerization, 2-hydroxyethylacrylate, ethylacrylate, interpolymer complexes, lower critical solution temperature.

Introduction

More and more attention of scientists of the world community is attracted by materials possessing a certain “memory” and capable of reacting to changing the parameters of the external environment according to a pre-programmed scheme. Such materials include water-soluble hydrophilic polymers [1] and, especially, their mesh analogs–polymer hydrogels, which are capable of retaining significant amounts of water in their structure. Researchers particular interest is stimulus-sensitive hydrogels capable of swelling and contracting when changing environmental parameters [2], such as temperature [3], pH [4], electric field, etc. Synthesis and investigation of the physico-chemical properties of stimulus-sensitive polymers appear to be important both from the point of view of understanding the features of structure formation and in terms of creating polymer reagents for various purposes. Areas of practical application of hydrophilic polymers are very numerous and diverse: medicine (controlled injection and isolation systems, dressings, contact lenses, construction materials for endoprosthetics, contraceptives, transplantation in cell therapy, etc.) [5-7], agriculture (hydroabsorbents for regulation of water regime of soils) [8], biotechnology (concentration, purification, utilization of biological objects) [9], robotics (artificial muscles), etc.

The development of the fundamental foundations for the creation of such polymers is very relevant in connection with the broad prospects of their practical application. The thermo- and pH-sensitivity of the swelling polymer networks can be realized with a certain hydrophilic-hydrophobic balance of the macrochains of the nets. The given balance, in turn, is provided by the ratio of hydrophilic and hydrophobic monomers participating in the copolymerization reaction in the synthesis of the copolymer. The hydrophobicity is generally the hydrocarbon chains of alkenes, dienes, alkyl methacrylates, hydrophilicity–sections of macrochains containing heteroatoms, hydrophilic or ionogenic groups. The most investigated hydrophilic polymers include, for example, ethylene glycol monomethacrylate, 2-hydroxyethylacrylate (HEA)-VBE [10], HEA- butylacrylate [11], hydroxyethylacrylate (HEA)-hydroxyethylmethacrylate [12] (2-hydroxyethyl acrylate). A similar ester of acrylic

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acid in the creation of stimulus-sensitive nets was not investigated. Although, in this monomer, the absence of a β-methyl group makes it possible to reduce hydrophobicity.

In the recent years the researchers have showed a special interest in thermosensitive copolymers the aqueous solutions of which possess lower critical solution temperature among water-soluble polymers. Currently, most of them have already been used in biomedicine to provide the controlled delivery of drugs, in tissue engineering, food industry, electronics and etc.

However, the range of available thermosensitive polymers is quite limited and besides the main part of papers is devoted to poly-N-isopropylacrylamide and polymers of polyethylacrylate are investigated to a much lesser extent [13]. In the present paper the approach based on radical copolymerization of monomers with a significant difference in the hydrophobic-hydrophilic balance of chemical structure was used to synthesize novel thermosentitive polymers. It allows regulating the ratio of hydrophobic and hydrophilic components in macrochains, and respectively, the temperature of phase transitions in polymer-water system in wide ranges [14]. The important thing is that monomers, homopolymers, which do not have LCST in aqueous solutions can be used starting materials for such copolymers. In the present paper to synthesize stimulus-sensitive copolymers we used 2-hydroxyethyl acrylate as a hydrophilic monomers and ethylacrylate was as a hydrophobic monomer.

Materials and methods

2-hydroxyethylacrylate (HEA) (Sigma Aldrich (UK)) contained 96% of basic product. It was purified by double vacuum distillation in argon flow (b.p.=91^0/12 mm. sec., n_D^{20}=1.4500).

Ethylacrylate (EA) (Fisher Scientific (UK) contained 96% of basic product. It was washed by 10 % water KOH solution from inhibitor, was dried above potash and was purified by double vacuum distillation (b.p.=99^{0}C, T_i=71^{0}C, n_D^{20}=0.9405).

Azo-bis-iso-butyric acid dinitrile (ABAD) of “c” grade (Acros (USA) was twice recrystallized from absolute methanol, m.p.=103^{o}C.

Ethanol (absolute with m.p.=78^{o}C/760 mm. Hg, n_D^{20}=1.3612-1.3618) was produced by Sigma-Aldrich Co. (USA).

To prepare solutions the distilled water was used.

Synthesis of HEA-EA copolymers of linear and crosslinked structure.

Water-soluble linear (co)polymers of HEA-EA with composition 90:10%; 80:20%; 70:30%; 60:40%; 30:70%; 20:80%; 10:90% were synthesized using the method of radical copolymerization of 50% solution of HEA:EA mixture of various compositions in ethanol at 60°C. Copolymerization was carried out in the ampoules of molybdenum glass. Reaction mixtures were blown off by argon for 20 minutes to remove oxygen from reaction mixture. The substance radical polymerization of liner EA and HEA monomers was initiated by thermal decomposition of azo-bis-iso-butyric acid dinitrile. The resulting linear copolymers were poured into the dialysis membrane to purify from unreated monomers. The samples obtained were dried by liophylization up to a constant weight and then aqueous solutions were prepared.

Physico–chemical methods of investigation of polymers.

The composition of the HEA-EA copolymers was determined by ^{1}H NMR spectroscopy in deuterated dimethylsulfoxide (DMSO-d_6) using NMR spectrometer (Bruker DPX-400 (400 MHz) (UK) at 293 K. All chemical shifts were recorded as δ in parts per million (ppm), and references to the residual solvent signal ((CD_3) SO: ^{1}H, δ=2.50 ppm) were recorded too.

IR spectra of initial samples of polymers was recorded on a spectrophotometer (Perkin-Elmer FTIR Spectrum Two (UK) in the region of 400-4000 cm^{-1}. Samples were prepared in the form of tablets with KBr.

The optical density of solutions of polymers was determined on the UV spectrophotometer (Shimadzu UV/ VIS-2401 PC (Japan)) at a wavelength of 400 nm.

The effect of the temperature on aggregation behavior and phase diagrams of the solutions of polymers were investigated by determining the cloud points on UV-spectrometer with the help of thermostat cell using thermo-electronic cuvette regulator (CPS-240A Shimadzu (Japan)).

Thermal analysis of (co) polymers was carried out using a thermogravimetric analyzer on the instrument (Perkin Elmer Pyris 1 TGA (Perkin Elmer Instruments (UK) at a heating rate of 10°C/min in a dry nitrogen atmosphere (99.99%, flow rate 20 ml/min). The mass of polymer samples in isopoly acid was about 10-12 mg. The experiments on differential–scanning calorimetry of the samples were carried out on the instrument (Perkin Elmer Diamond DSC by Perkin Elmer Instruments (UK) at scanning rate of 10^{o}C/min in the atmosphere of dry nitrogen. As the parameters of thermoanalysis, particularly glass point, are sufficiently sensitive to the conditions of the experiment and the presence of moisture inside the polymers the system together with the samples were pre-heated up to 210^{o}C at the rate of 10^{o}C/min and then cooled at a rate of 10^{o}C/min. The second scanning was made as experimental data.

Liophylization. The samples were liophylized using Heto PowerDry® LL3000 connected to rotor lubricating pump (Edwards RV3) at -53°C.

The dialysis membranes (molecular mass of 12-14 kDa) were supplied by MediCell International Ltd company (UK).

Results and discussion

In the present paper to synthesize novel thermosensitive copolymers based on copolymerization of monomers with a significant difference in hydrophilic-hydrophobic balance of chemical structure was used. It allows regulating the ratio of hydrophilic and hydrophobic components in macrochains and, respectively, temperature of phase transitions in polymer-water system in wide ranges. Earlier Nurkeeva Z.S. et.al. effectively used this procedure when creating a wide range of novel thermosensitive polymers [14; 15]. Importantly, monomers, homopolymers, which do not have LCST can be used as starting materials. In the paper, for the first time, the synthesis of novel copolymers based on 2-hydroxyethylacrylate (HEA) and ethylacrylate (EA) was made by radical copolymerization. HEA–EA copolymerization was carried out in the presence of azo-bis-isobutyric acid dinitrile as an initiator.

To determine the chemical composition of the resulting copolymers ^{1}H NMR–spectroscopy was used. DMSO–d$_6$ was used as a solvent. The Figures 1 and 2 show ^{1}H NMR – spectra of poly-2-hydroxyethylacrylate (PHEA) and polyethylacrylate (PEA) for comparison. PEA: protons–CH$_3$ group of the basic chain (a and d) show resonance in the range of 1.1-1.2 ppm. Resonance signals of the protons of –CH- and –CH$_2$- groups of the basic chain (a and b) of 1.35-1.85 ppm and –CH$_2$- (c) methylene protons of homopolymer are observed at 2.1-2.3 ppm, 3.9-4.1 ppm, respectively. These data are well–correlated with PHEA NMR spectra data.

For PHEA (Figure 1) in NMR spectrum protons of -CH- and -CH$_2$- (a and b) groups of the basic chain exhibit resonance at 1.4-1.8 ppm and 2.15-2.3 ppm, respectively. The signals at 3.5-3.6 ppm and 3.9-4.1 ppm relate to -CH$_2$- protons of hydroxyethyl group (d and c) and resonance at 4.7-4.8 ppm corresponds to OH (f) of the group given above. These data are well-agreed with PHEA NMR spectrum data obtained by Coca et al. [16].

For copolymers obtained during the initial stages of conversion the composition was identified by ^{1}H NMR–spectroscopy. The composition was determined by the ratio of the integral intensities of NMR spectrum signals in the region of 4.70-4.81 ppm belonging to the position to protons of HEA hydroxyl group and also the intensity of the signals observed in the region of chemical shifts at 1.1-1.2 ppm typical of the protons of EA (Figure 3) end methyl group (DMSO–d$_6$ was used as a solvent).

As ^{1}H NMR spectra show (Figure 3) integration and account of the ratio of the intensity of signals observed in the region of chemical shifts at 3.6 ppm characteristic of PHEA methylene group and the signal in the region of 1.2 ppm relating to the protons of PEA –CH$_3$- group allowed determining the composition of copolymers (table 1) and calculating copolymerization constants *(r_1* and *r_2)* for monomers during copolymerization. Initial monomer mixtures, compositions of copolymers, their molecular–mass characteristics are shown in table1.

The processing of these data by Feynman-Ross (Figure 4) and Kelen Turdosa equations (Figure 5) has showed constants of copolymerization r_1(HEA)=0,46-0,3 and r_2(EA)=0,62-0,72 which indicate the higher reactivity of EA compared with the reactivity of HEA.

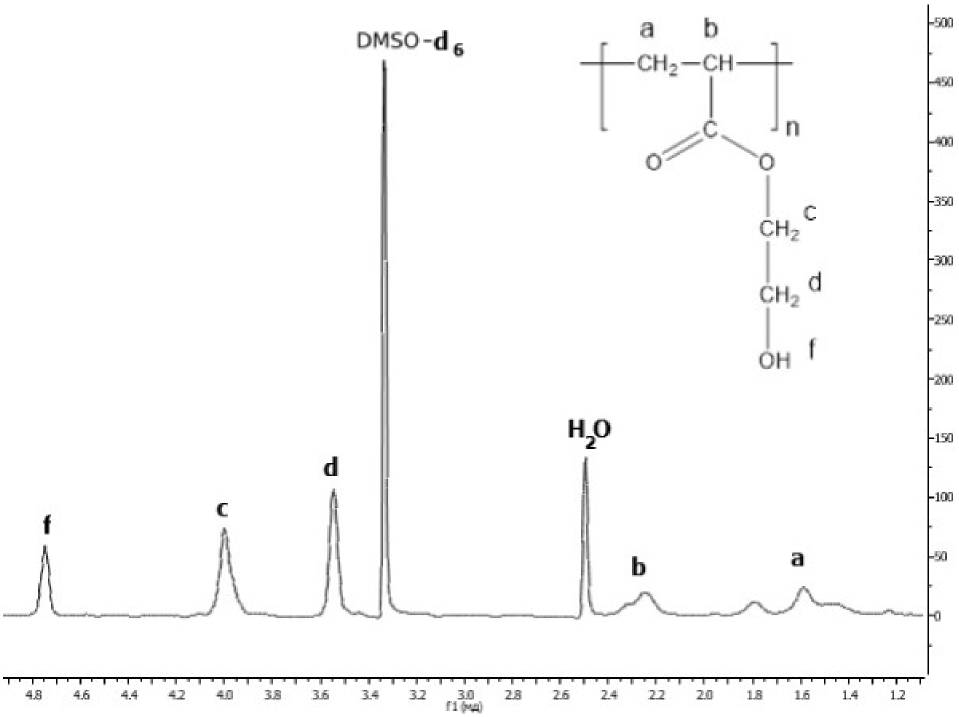


Figure 1 – ^{1}H NMR–spectra of poly-2-hydroxyethylacrylate (PHEA)

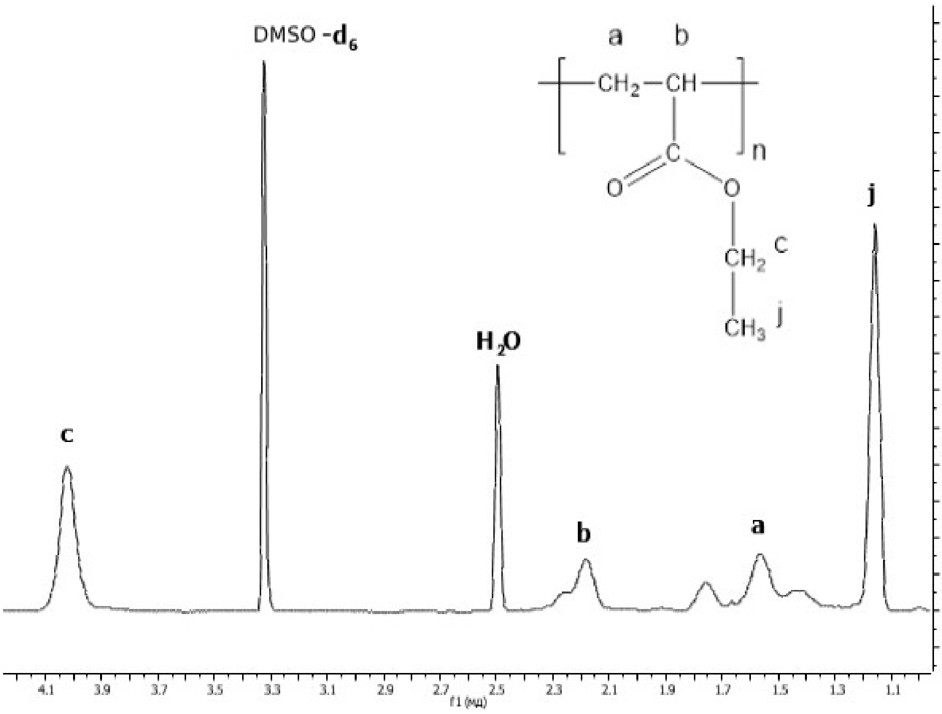
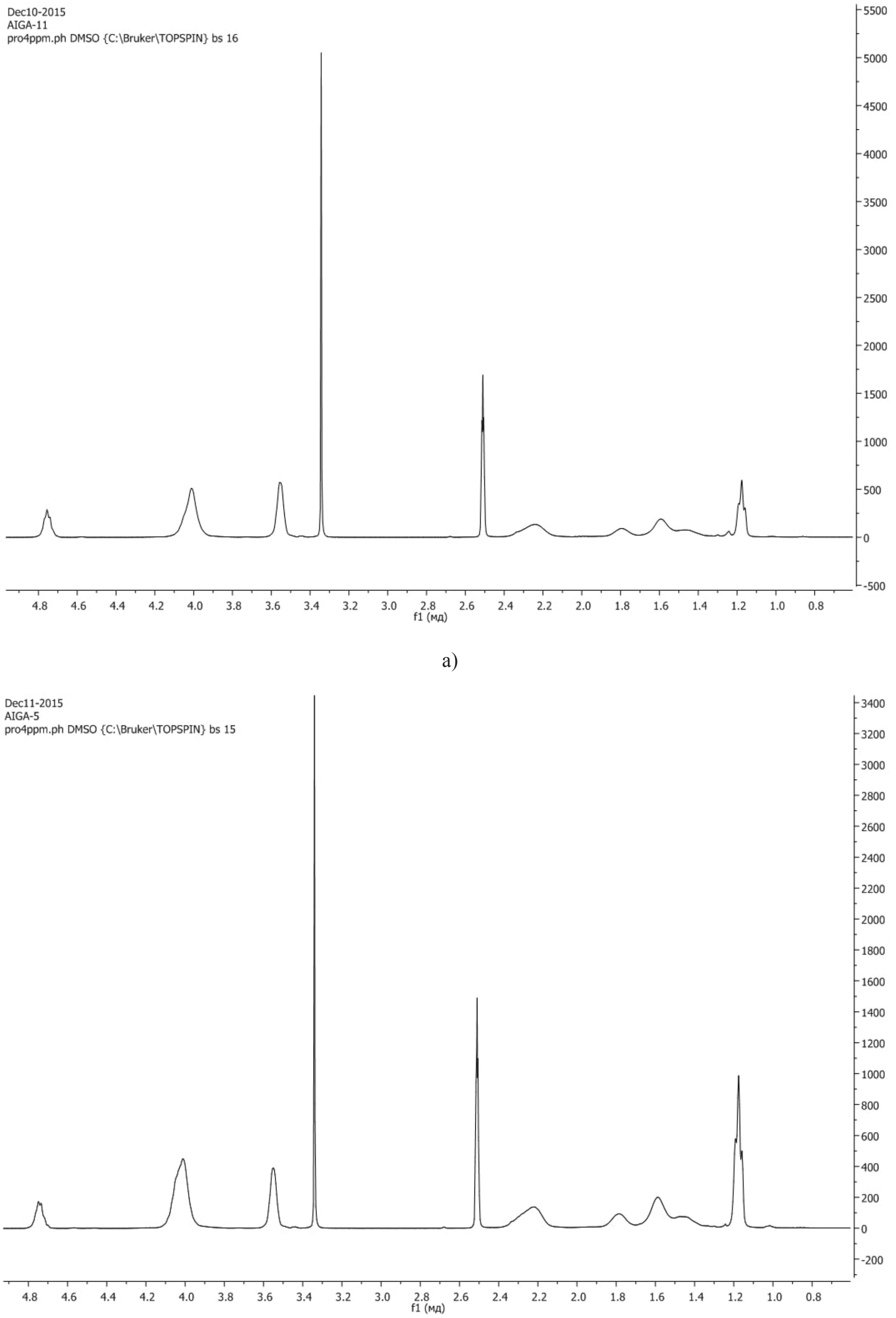


Figure 2 – ^{1} H NMR–spectra of polyethylacrylate (PEA)



a)

b)

IMM [HEA]:[EA]=70:30 (a); 30:70 (b) mol.%

Figure 3 – ^{1}H NMR–spectra of copolymers HEA:EA

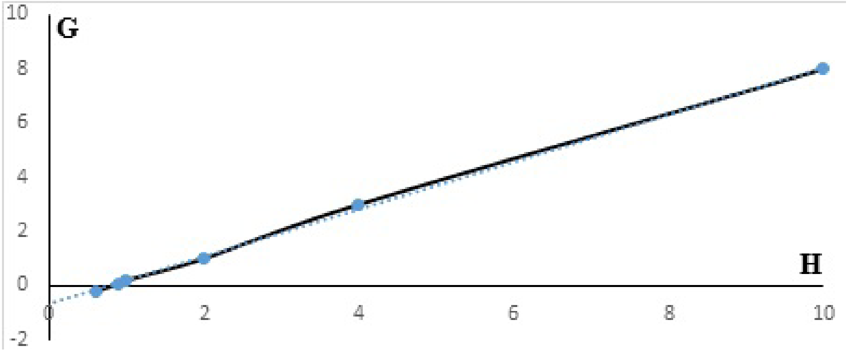


Figure 4 – Determination of the copolymerization constant by the Fayman-Ross method

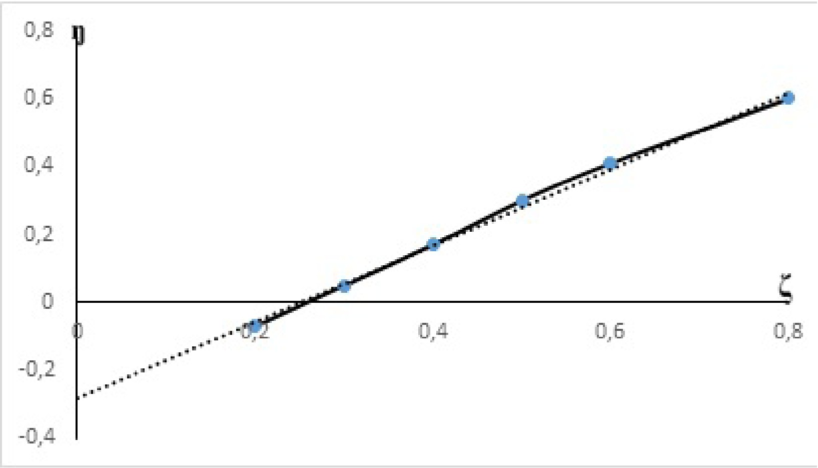


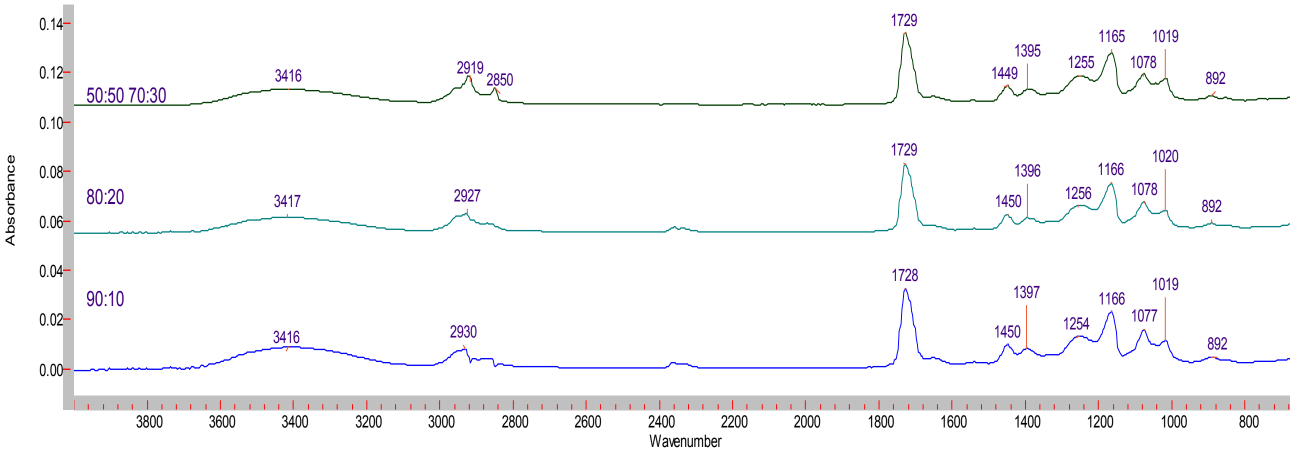
Figure 5 – Determination of the copolymerization constant by the Kelen Turdos method

Table 1 – Determination of constant of copolymerization based on HEA-EA with Feynman-Ross and Kelen-Turdosa method

IMM [HEA]:[EA] mol.%		Composition of the copolymer [HEA]:[EA] мол.%		$F= M_1 / M_2$	$f= m_1 / m_2$	$G=F(f-1)/f$	$H=F^2/f$	$\eta=G/(\alpha+H)$	$\zeta=H/(\alpha+H)$	The copolymerization constant	Fineman-Ross(FR)	Kelen-Turdos(KT)
M_1	M_2	m_1	m_2									
90	10	88,78	11,22	9	7,913	7,863	10,237	0,619	0,806	r_1	0,46	0,3
80	20	80,12	19,88	4	4,030	3,008	3,970	0,468	0,617			
70	30	69,72	30,28	2,33	2,303	1,318	2,358	0,273	0,489	r_2	0,62	0,72
60	40	63,33	36,67	1,5	1,727	0,631	1,303	0,168	0,346			
50	50	51,47	48,53	1	1,061	0,057	0,943	0,017	0,277			
40	60	43,10	56,90	0,67	0,758	-0,214	0,593	-0,070	0,194	r_1*r_2	0,29	0,22

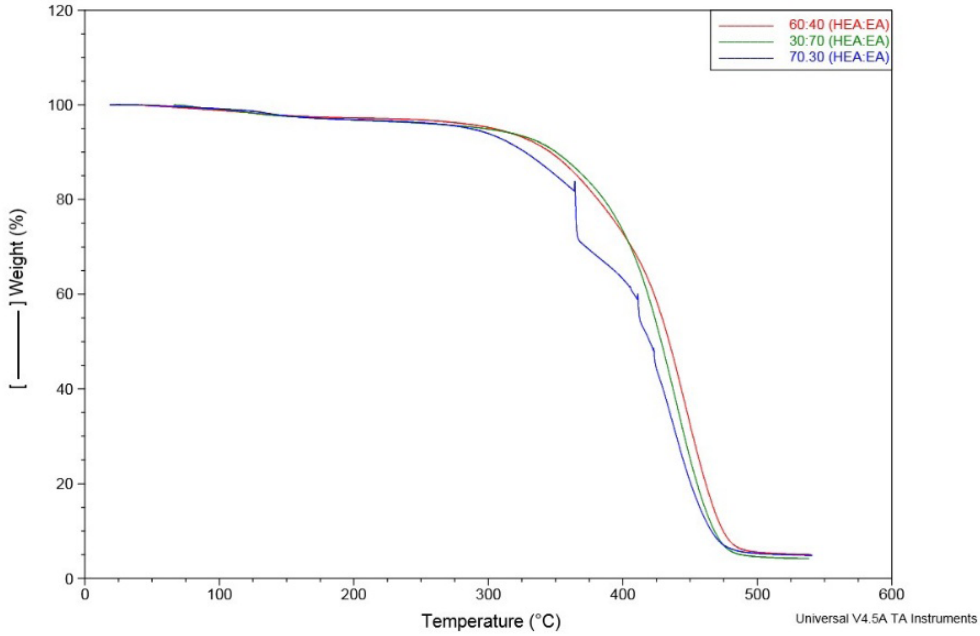
$$\alpha(H_{max}H_{min})^{1/2}=2.463$$

For synthesized copolymers based on HEA and EA IR-spectra (400-4000 cm^{-1}) were recorded. Figure 6 shows IR-spectra of HEA-EA copolymers of a various composition. The following signals allowed identifying functional groups of HEA-EA copolymers of –CH_3- group 1019-1078 cm^{-1}, –CH_2- group (1165-1256 cm^{-1}), –CH- group (1395-1450 cm^{-1}), C=O (1729 cm^{-1}) and HEA components of –CH_2- (2850cm^{-1}) which are next to hydroxyl group 3417 cm^{-1} respectively.



IMM [HEA]:[EA] = 90:10; 80:20; 70:30 mol.%

Figure 6 – IR spectra of copolymers of HEA-EA



IMM [HEA]:[EA]=70:30 (1); 60:40 (2); 30:70 (3) mol.%

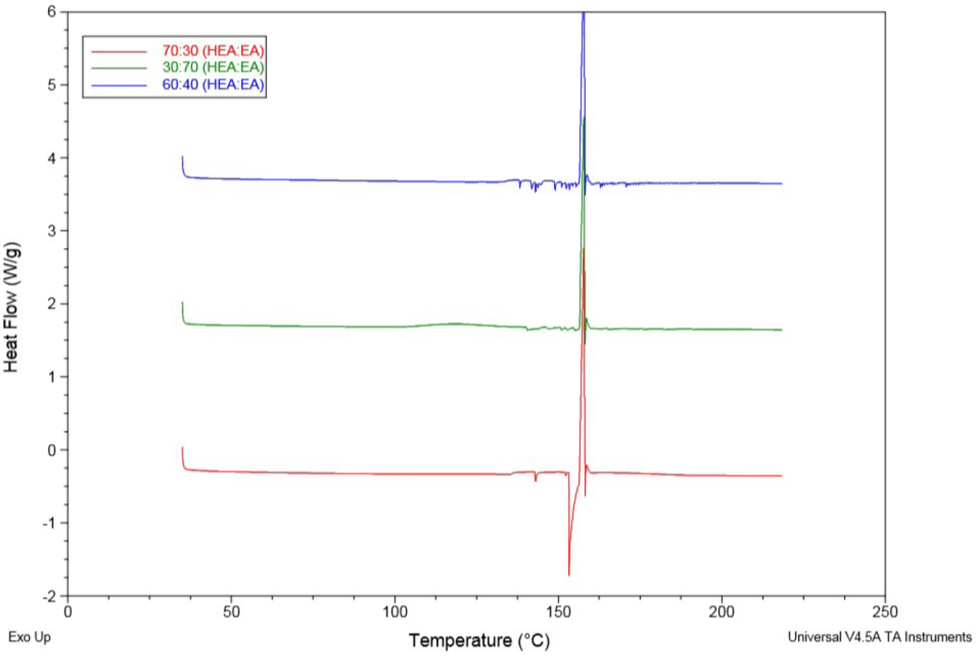
Figure 7 – TGA curves for HEA-EA copolymers

Figure 7 shows the data of thermogravimetric analysis (TGA) of the samples of HEA-EA copolymers of a various composition. Destruction of copolymers consists of two stages. The initial loss of weight is observed at about 50-225°C. It is conditioned by releasing air moisture absorbed. The final and complete loss of the weight of copolymers up to 90% starts at about 470ºC and reaches maximum at 482ºC that causes the complete degradation of copolymers. In general, the absence of apparent inflections evidence that the samples don't contain low-molecular impurities including solvent of oligomer.

To study the compatibility of HEA-EA copolymers in details their *standard temperatures were determined using the instrument of differential-scanning calorimetry (DSC)*. Figure 8 shows DSC analysis results of HEA-EA copolymers, respectively. These figures show that there is one transition from glass state to high-elasticity in thermographs at that standard temperature shifts to the region of lower values with decreasing HEA content in the copolymer composition. The data of standard temperatures obtained by theoretical and experimental calculations are given in table 2. DSC analysis data confirm the value of standard temperature for copolymers with theoretically-calculated data.

For novel linear HEA and EA copolymers hydrodynamic behavior in the solution at temperature variation was studied using turbidimetry (Figure 9-11). It is seen that when temperature increases the solutions of HEA-EA copolymers grow turbid in a narrow range. It indicates their thermosensitive properties i.e. Lower critical solution temperature (LCST) is typical of copolymers (CPL) above of which layer separation occurs. At that when the concentration of the solutions increases phase transition shifts to the region of low values which is obviously connected with worsening the thermodynamic quality of a solvent due to the destruction of hydrogen polymer-solvent bonds and also to the enhancement of hydrophobic interactions of EA components.

In the paper temperature of phase transition of the solution of copolymers based on HEA-EA was found not to exhibit thermosensitivity when the content of EA components decrease (figure 10) by 10% mol. The data obtained are well-agreed with the results of the paper [17] which shows that when the content of the components of NIPAAM monomer increases in the copolymer composition temperature of phase transition of the solutions of copolymers based on HEA-EA decreases.

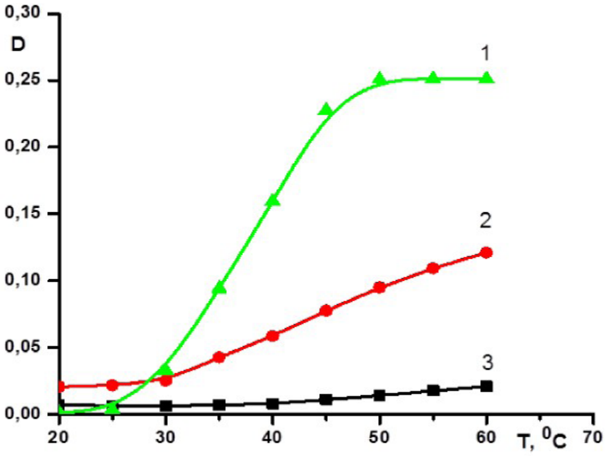


IMM [HEA]:[EA]=70:30 (1); 60:40 (2); 30:70 (3) mol.%

Figure 8 – DSC curves for HEA-EA copolymer

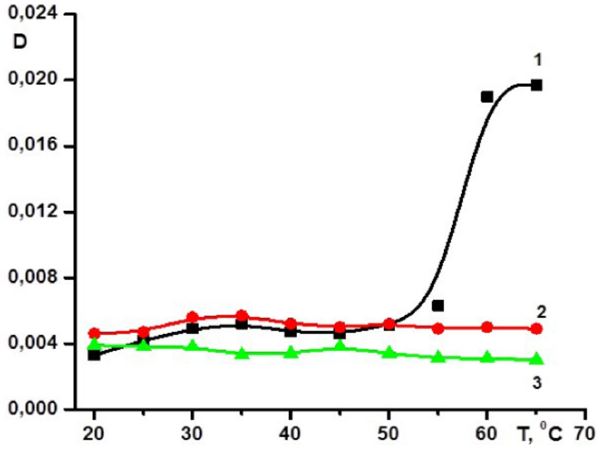
Table 2 – Thermal characteristics based on HEA-EA

[HEA-EA] мол.%.	$T_{st.}$, °C	Temperature, °C	Loss of mass, %	The remainder of the mass, %	PDT_{max}, °C
30:70	158	90-175 345-600	1.98 93	98.02 5,02	482
60:40	156	50-200 340-600	4.99 92	95.01 3	477
70:30	152	130-225 341-600	5.98 91.5	94.02 2.52	470



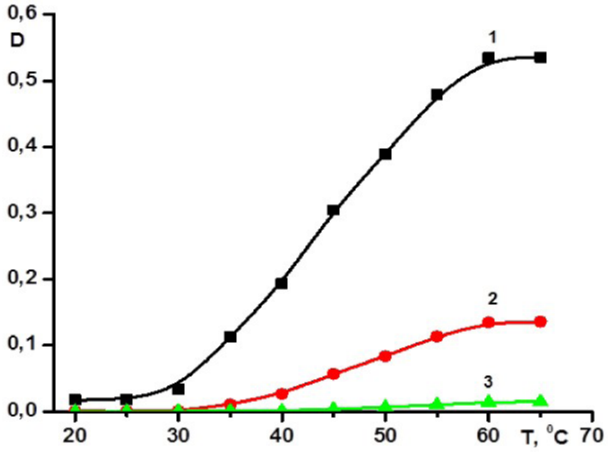
IMM [HEA]:[EA]=70:30 mol.%;
[HEA:EA]=0.05 (1); 0.025 (2); 0.01% (3)

Figure 9 – Dependence of optical density of aqueous solutions of linear copolymers of HEA-EA on temperature



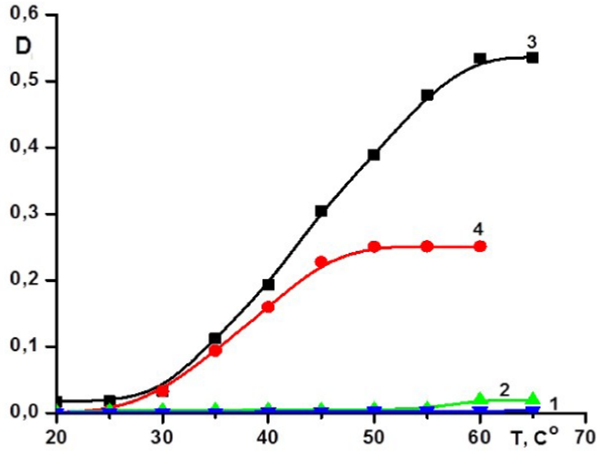
IMM [HEA]:[EA]=90:10 mol.%;
[HEA:EA]=0.05 (1); 0.025 (2); 0.01% (3)

Figure 11 – Dependence of optical density of aqueous solutions of linear copolymers of HEA-EA on temperature



IMM [HEA]:[EA]=80:20 mol.%;
[HEA:EA]=0.05 (1); 0.025 (2); 0.01% (3).

Figure 10 – Dependence of optical density of aqueous solutions of linear copolymers of HEA-EA on temperature



PHEA (1); IMM [HEA]:[EA]=90:10 (2);
80:20 (3); 70:30 (4) мол.%;
[HEA:EA]= 0.05%

Figure 12 – Dependence of optical density of aqueous solutions of linear copolymers of HEA-EA on temperature

In the paper the effect of the composition of copolymers on temperature was also studied (figure 12). When the content of EA fragments increases in copolymer composition phase transition of the aqueous solutions of copolymers from a globule to a coil occurs within a lower temperature range and the aqueous solution of homoHEA doesn't exhibit thermosensitivity [18].

Conclusion

For the first time, thermosensitive polymers hydrogels based on 2-hydroxyethyl acrylate (HEA) and ethyl acrylate (EA) have been synthesized by radical copolymerization.

To determine the physicomechanical properties of a copolymer IR-, ^{1}H NMR-, UV- spectroscopy, thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), turbidimetry was used.

To determine the compositions of copolymers and relative activities of comonomers were calculated. The study of phase diagrams of the aqueous copolymer solutions showed LCST presence the value of which rises with increasing the content of HEA components in the composition of copolymers.

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