CELLULOSE CHEMISTRY AND TECHNOLOGY

FUNCTIONALIZATION OF CELLULOSE:
SYNTHESIS OF WATER-SOLUBLE CATIONIC CELLULOSE DERIVATIVES

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One of the trends of modern cellulose chemistry is the functionalization of known cellulose derivatives in order to expand their application area. In this work, water-soluble cationic cellulose derivatives containing up to 4% coupled nitrogen were obtained by the amination of hydroxyethylcellulose (HEC) with two different etherification agents, diethylepoxypropylamine (DEEPA) and (2-chlorethyl) diethylamine hydrochloride (DEAE). The influence of the composition of the reaction mixture on the degree of substitution was investigated by using mathematical planning of the experiments and was described by regression equations. The effect of the etherification agent on the composition of cationic groups of the obtained derivatives was examined. It was found that the HEC reaction with DEEPA resulted in a monofunctional cationic polyelectrolyte containing tertiary amino groups, which could be assigned to cationic groups of intermediate basicity (pK_a approx. 8.2). On the contrary, the amination of HEC with DEAE gave polyfunctional derivatives containing a mixture of weakly and intermediately basic amino groups with pK_a 6.0-6.2 and 8.2-8.6, respectively. The synthesized derivatives are soluble in polar aprotic solvents, as well as in water, and the solutions possess high stability at elevated temperature and a high concentration of salts.

Keywords: cellulose derivatives, aminocellulose, cationic polyelectrolytes, water-soluble polymers, cationic cellulose derivatives

INTRODUCTION

The methods used for the synthesis of water-soluble cellulose derivatives could be divided into conventional and unconventional ones. Unconventional methods for the chemical modification of cellulose are thoroughly discussed in reviews.[1,2] The methods for derivatization of cellulose implemented in the industry could be attributed to traditional ones. Most of them are based on etherification *via* the reaction of cellulose hydroxyl groups with epoxy-compounds or alkyl halides. The reactions are performed under heterogeneous or homogeneous conditions. Native cellulose is not soluble in water and common organic solvents due to its highly ordered hydrogen bond network. Recently, a lot of new solvent systems, such as ionic liquids,[3,4] mixtures of aprotic dipolar solvents with lithium chloride,[5] NaOH/urea[6] have been studied and used for the homogeneous modification of cellulose. However, their industrial application is problematic.

One of the trends of modern cellulose chemistry is the functionalization of known cellulose derivatives.[7] Such a way allows to combine different functional groups with controlled composition in order to give the products new favourable properties and thus to expand their application area. In this case, the functionalization reaction may be performed in a solvent of a raw cellulosic material. Such a cellulose functionalization approach is successfully used in many works.[8-11] The effect of different functional groups and their amount on the physical, chemical properties, solubility, biological activity, and biodegradability of the derivatives has been studied.

Water-soluble cationic cellulose derivatives are of special interest. Being ‘smart’ polyelectrolytes, they show sensitivity to pH and ionic strength variations. They could find application in drug[12-14] or gene[6,15,16] delivery systems. It has been shown[14] that cationic cellulose derivatives have potential to be used for controlled delivery of drugs of acidic character. Prolonged drug release is achieved due to the ionic interaction between amino groups of a cellulose derivative and acidic ones of the drug. The cationic derivatives are also used as flocculants for waste water treatment and as additives in papermaking, as thickeners for mineral processing and oil recovery, as conditioners in hair care formulations.[5,17,18] Due to their positive charge, cationic polyelectrolytes are used for coating of the negatively charged silica surface in order to enhance its biocompatibility, for example, preparing stationary phases for HPLC or GC.[19,20]

Water-soluble quaternized cellulose derivatives produced by etherification of cellulosic material with quaternary halohydrins or quaternary epoxides are well known and possess some valuable properties (see review)[7]. However, in some cases a strong basic character of such derivatives limits their application. It is known that the derivatives containing strong basic groups cause irritation of skin and mucosa. Thus, basic cationic derivatives with tertiary amino groups of intermediate basicity are often preferable for biomedical or pharmaceutical applications and for cosmetic formulations. There are very few methods for the preparation of cationic cellulose polyelectrolytes of intermediate basicity[21,22] and they have some drawbacks.

The aim of this work was to obtain water-soluble cationic cellulose derivatives containing tertiary amino groups by means of two different approaches. For this purpose, the etherification of hydroxyethylcellulose (HEC) with two different etherification agents, diethylepoxypropylamine (DEEPA) and (2-chlorethyl) diethylamine hydrochloride (DEAE), was studied. Special attention has been focused on the effect of the etherification agent on the composition of cationic groups of the obtained products.

EXPERIMENTAL

Materials

Hydroxyethylcellulose (HEC) having 32% of coupled ethylene glycol (MS approx. 1.7) was obtained from Polimersintez, Russia. (2-chlorethyl) diethylamine hydrochloride (DEAE) was purchased from Sigma-Aldrich, diethylepoxypropylamine (DEEPA) was synthesized according to Gilman.[23] All other chemicals were of reagent grade.

Aminoalkylation of HEC with DEEPA

The HEC was dissolved in water and a required amount of DEEPA was added. The mixture was stirred at an elevated temperature. The product obtained (DEEPA-HEC) was precipitated in acetone or acetone-diethyl ether mixture and thoroughly washed with ethanol.

Aminoalkylation of HEC with DEAE

The HEC was dissolved in water and a required amount of DEAE and NaOH was added. To prevent the oxidation of cellulose, 0.01 mg of sodium borohydride was added per gram of HEC. The reaction was performed at 50 °C for 30 min under stirring. Aminated HEC (DEAE-HEC) was precipitated twice in acetone and thoroughly washed with ethanol. In some cases, aminocellulose was additionally purified by ultrafiltration of its solution in water on Amicon ultrafiltration apparatus (USA), using a 10000 MW membrane.

Chemical characterisation of the products

The content of coupled nitrogen N was determined according to the Kjeldahl method. The degree of substitution DS was calculated using the equation:

$$DS = \frac{238 \cdot N}{1400 - MM_{group} \cdot N}$$

where 238 – molar mass of the anhydroglucose unit of HEC; MM_{group} – molar mass of the diethylaminohydroxypropyl or diethylaminoethyl group, which is equal to 130 and 100, respectively; 1400 – (nitrogen atomic mass) x 100.

Structural characterization of aminocelluloses

FT-IR spectra were recorded by a FT-IR Spectrum GX spectrometer (Perkin Elmer). Raman spectra were obtained with Vertex 70v spectrometer (Bruker) equipped with a Ram II module.

Potentiometric titration

Potentiometric titration was carried out with 0.05 mol L^{-1} HCl at 25 °C, using a 744 pH-meter (Methrom, Switzerland). The ion-exchange capacity was calculated from equivalence points. The equivalence points for each type of amino group were determined graphically from tangential lines drawn through inflection points, using standard procedures. The pK_a value of a charged group was calculated by the equation of

Hendelsson-Haselbach at a dissociation degree α = 0.5.

All solutions were prepared in deionised and degassed water, which was obtained through boiling and subsequent cooling under nitrogen atmosphere.

Solubility of aminocelluloses

The solubility of cellulose derivatives in different solvents was determined at 20 °C, and the polymer concentration was approx. 1%. The tolerance of cellulose derivatives for salts was determined by gradually adding the salt to 1% solution of the derivative till the precipitation of the polymer.

The cloud point of the solution, i.e. the lowest temperature at which turbidity was developed, was evaluated at different pH, gradually heating the solution. The heating rate was of 0.5 °C min^{-1}. In the work reported here, the cloud point was determined visually.

RESULTS AND DISCUSSION

One of the approaches for the preparation of water-soluble cationic cellulose derivatives is the functionalization of water-soluble non-ionic cellulose derivatives using etherification agents containing amino moieties. For this purpose, water-soluble hydroxyethylcellulose was used as a raw cellulosic material, and diethylepoxypropylamine (DEEPA), as well as (2-chlorethyl) diethylamine hydrochloride (DEAE) were used as etherification agents. It should be mentioned that DEEPA is not stable during long storage, thus it was not purchased but synthesized in the laboratory. On the contrary, DEAE is a commercial reagent widely used on industrial scale.

Amination of HEC with DEEPA

Amination of HEC with DEEPA was performed in aqueous medium according to the well-known ring-opening reaction of epoxide (Fig. 1). Etherification of cellulose with epoxy-compounds usually is performed under alkaline conditions, where alkali plays the role of catalyst. Using DEEPA in OH^- form as an etherification agent, the reaction does not require any additional catalyst, because in the presence of water it is catalysed *in situ* by tertiary amines.

The limiting concentration of the reaction components for obtaining water-soluble aminocellulose were found to be following: 3.5-7.7% HEC, 1.0-43.5% DEEPA and 52.4-93.8% water. The diagram presented in Fig. 2 indicates the composition of the reaction components, giving water-soluble aminated products at a reaction temperature of 100 °C. The lowest concentration of water is limited by the high viscosity of the HEC solution; the highest one is determined from the economical point of view. The preferable ratio water:HEC is 9:14 (w/w). The highest concentration of DEEPA in the reaction mixture is restricted due to the limited solubility of HEC in the DEEPA:water mixture. If the ratio DEEPA:water exceeds 0.83 (w/w), HEC precipitates from the solution.

The reaction kinetics was studied in the range of the reaction temperature between 40 °C and 100 °C, keeping constant the ratio HEC:H_2O:DEEPA at 1:12:3 (w/w). Kinetic curves are given in Fig. 3. The results show that the reaction rate is dependent on temperature. The highest substitution degree is obtained in 0.5, 1, 2 and 3 hours at temperatures of 100, 80, 60 and 40 °C, respectively.

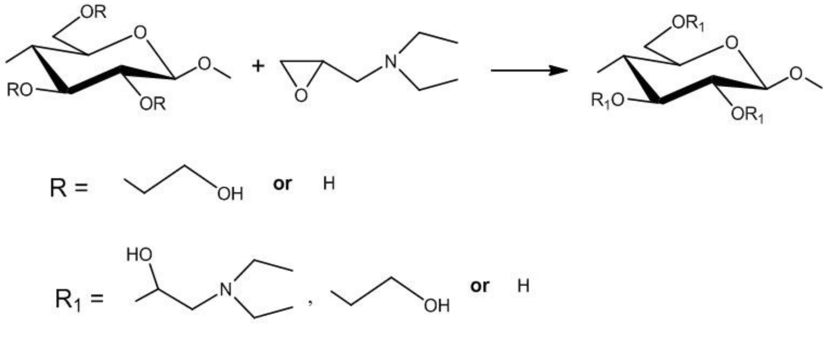

Figure 1: Scheme of the reaction of HEC with DEEPA

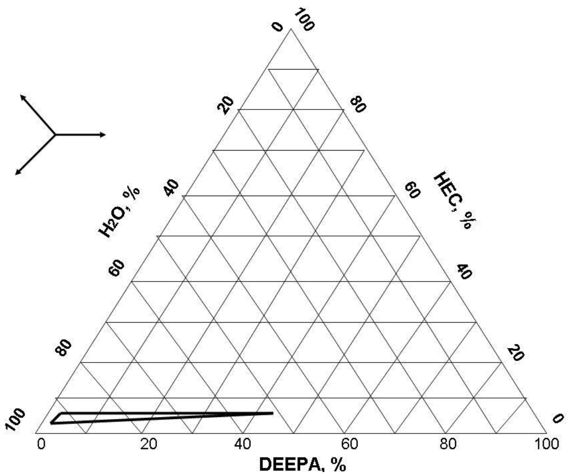

Figure 2: Diagram of the composition of the reaction components for obtaining water-soluble aminocellulose (reaction temperature: 100 °C)

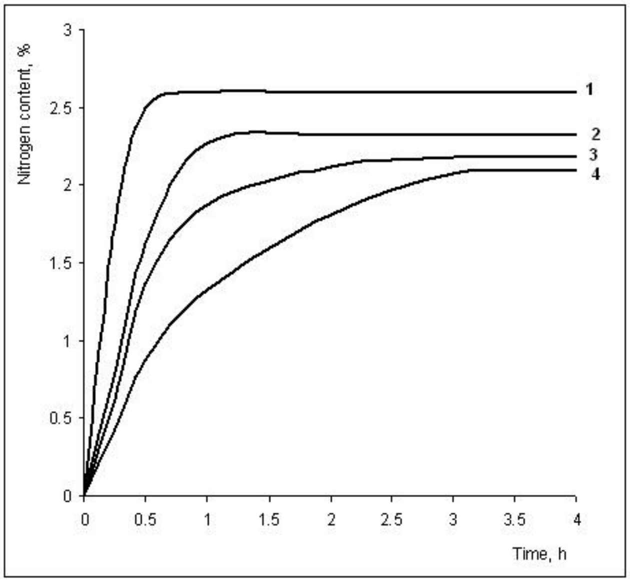

Figure 3: Kinetic curves of HEC reaction with DEEPA at temperatures of 100 °C (1), 80°C (2), 60 °C (3), 40 °C (4); ratio of HEC:H_2O:DEEPA = 1:12:3 (w/w)

The interaction of HEC with DEEPA was investigated by using mathematical planning of the experiments.[24] The experiments were designed according to the first-order orthogonal plan. Matrices of the two-level full factorial design are presented in Tables 1 and 2. The experiments were performed changing the ratio DEPPA:HEC (Z_1) in the range 0.2-10, that of water:HEC (Z_2) between 12-18, and the reaction temperature (Z_3) between 40-100 °C. The time of the reaction was the same in all the experiments and equal to 1 hour. The adequacy of the coefficients of the calculated regression equations was checked in accordance with the Student criteria. It was found that the reaction could be described by the following regression equations:

$$Y= 0.077+0.379Z_1-0.0001Z_2+0.0004Z_3-0.0222Z_1Z_2 +0.0075Z_1Z_3 \tag{1}$$

$$Y=0.3601+0.144Z_1-0.0496Z_2+0.0241Z_3 \tag{2}$$

where Y is the nitrogen content, %.

Equation (1) is applicable in the ranges: $Z_1 = 0.2\text{-}3$; $Z_2 = 12\text{-}18$; $Z_3 = 40\text{-}100$ °C, and equation (2) is adequate when $Z_1 = 3\text{-}10$; $Z_2 = 14\text{-}18$; $Z_3 = 40\text{-}100$. In practice, the equations serve to choose the proper composition of the reaction mixture for obtaining a cellulose derivative of a desirable substitution degree.

Graphically, the dependence of the nitrogen content on the reaction mixture composition is presented in Figures 4 and 5.

Table 1

Matrix of the full factorial design of the experiment at low ranges of the ratio DEEPA:HEC

Experiment	Factors on natural scale			Nitrogen content, %	
	DEEPA:HEC Z_1	Water:HEC Z_2	Temperature, °C Z_3	$Y_{experimental}$	$Y_{calculated}$
1	0.2	12	40	0.17	0.17
2	0.2	12	100	0.29	0.29
3	0.2	18	40	0.15	0.15
4	0.2	18	100	0.26	0.26
5	3.0	18	100	2.25	2.30
6	3.0	18	40	0.98	0.93
7	3.0	12	100	2.76	2.70
8	3.0	12	40	1.28	1.33

Table 2

Matrix of the full factorial design of the experiment at high ranges of the ratio DEEPA:HEC

Experiment	Factors on natural scale			Nitrogen content, %	
	DEEPA:HEC Z_1	Water:HEC Z_2	Temperature, °C Z_3	$Y_{experimental}$	$Y_{calculated}$
1	3	14	40	1.06	1.06
2	3	14	100	2.45	2.51
3	3	18	40	0.98	0.86
4	3	18	100	2.25	2.30
5	10	18	100	3.35	3.32
6	10	18	40	1.78	1.87
7	10	14	100	3.60	3.52
8	10	14	40	2.05	2.07

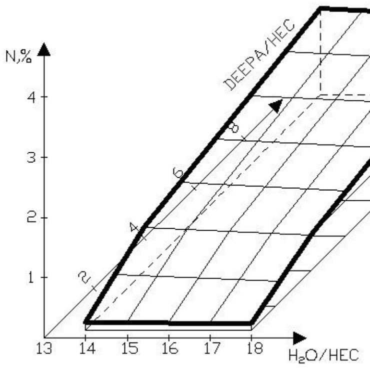

Figure 4: Dependence of nitrogen content in DEEPA-HEC on composition of the reaction mixture (reaction temperature: 40 °C)

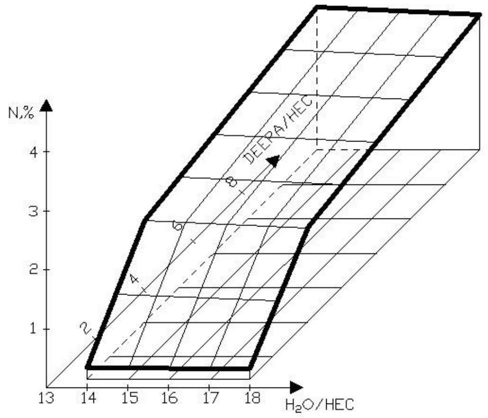

Figure 5: Dependence of nitrogen content in DEEPA-HEC on composition of the reaction mixture (reaction temperature: 100 °C)

The products containing up to approx. 4% of nitrogen (DS 1.08) may be obtained by the amination of HEC with DEEPA. The products with higher DS are not soluble in water and form a gel.

Amination of HEC with DEAE

The reaction of fibrous or microgranular cellulose with (2-chlorethyl) diethylamine hydrochloride (DEAE) is well-studied, and the derivatives obtained are well-known as anionexchangers, which are widely used in the chromatography of proteins. In this work, water-soluble HEC was used as cellulosic material. The amination reaction was performed under homogeneous conditions in water. In the case of DEAE, sodium hydroxide was added to neutralize the hydrochloride. The lowest ratio of NaOH to DEAE is the stoichiometric ratio of those reagents (equal to 0.233 g/g), but the optimal ratio ranges between 0.3-0.4. The reaction was performed at 50 °C for 30 min, according to the scheme presented in Fig. 6.

Fig. 7 shows the dependence of the nitrogen content in the cationic cellulose derivative on the ratio DEAE:HEC (w/w). The nitrogen content of the resulting derivatives is up to 4% (the substitution degree by amino groups is up to 0.95).

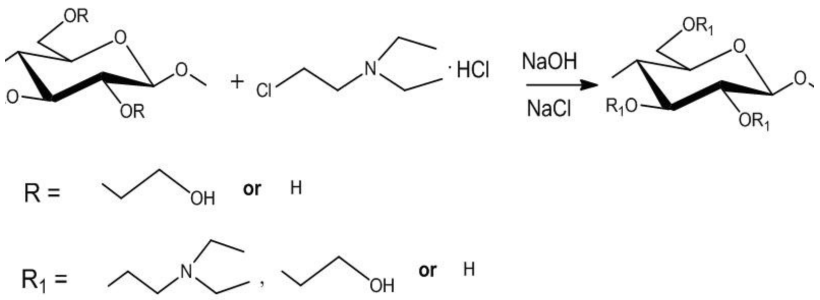

Figure 6: Scheme of the reaction of HEC with DEAE

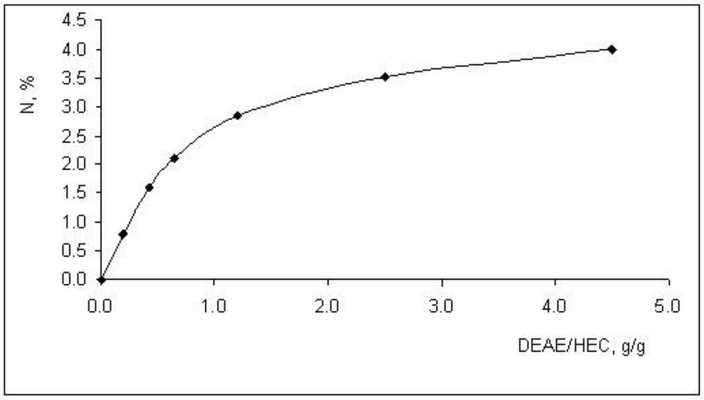

Figure 7: Dependence of nitrogen content in the cationic cellulose derivative on DEAE:HEC ratio (w/w); reaction temperature: 50 °C; ratio NaOH:DEAE = 0.35

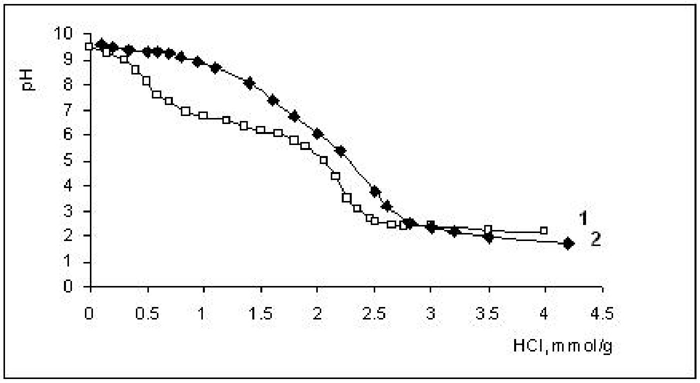

Figure 8: Potentiometric titration of aminocelluloses: 1- DEAE-HEC-3.4; 2- DEEPA-HEC-4.0

Purification of the products

Usually, the purification of water-soluble polymers is not an easy task. In the case of HEC amination with DEAE, besides the resulting cellulose derivative, an excess of NaOH is present in the reaction mixture. Moreover, after the reaction sodium chloride is found in the mixture, which is formed by the neutralization of hydrochloride with NaOH, as well as by-products of DEAE hydrolysis. Hydrolysed DEAE could be easily washed with organic solvents. However, due to the limited solubility of NaOH and NaCl in organic solvents, it is problematic to separate them from the cellulose derivatives. Such inorganic compounds were removed by thorough washing of precipitated aminocellulose with ethanol. In some cases, aminocellulose was purified by precipitation in acetone and subsequent ultrafiltration of its solution in water. Thus, the purification of the product obtained by the reaction of HEC with DEAE is rather complicated.

In the case of the interaction of HEC with DEEPA, there are very few possible side reactions. The main side reaction could be the formation of diols from the interaction of DEEPA with water. Since the side products are soluble in organic solvents, it is quite easy to purify the resulting cellulose derivative by its precipitation in acetone and subsequent washing with alcohol. Thus, contrary to DEAE-HEC, the purification of DEEPA-HEC is much easier.

Composition of cationic groups

Considering the application possibilities of cationic polyelectrolytes, it is very important to know their charge at a different pH, which is dependent on the basicity of amino groups. The composition of the cationic groups of the products was analysed by potentiometric titration. As one can see from the shape of the curves given in Fig. 8 (curve 1), the products obtained by amination of HEC with DEEPA are monofunctional cationic polyelectrolytes. pK_α of amino groups is approx. 8.2, thus the groups are of intermediate basicity.

On the contrary, the reaction of HEC with DEAE results in polyfunctional cationic polyelectrolytes (Fig. 8, curve 2). The DEAE-HEC contains mostly weakly basic amino groups (Table 3). The composition of the cationic groups depends on the reaction conditions, particularly on the ratio of NaOH:cellulose (data not presented). As determined by Gubensek,[25] different amino groups are obtained according to the reactions from Fig. 9.

Table 3
Composition of cationic groups of DEAE-HEC

Aminocellulose	Nitrogen content, %	Amount of cationic groups, %		Dissociation constant, pK_a	
		Of intermediate basicity	Of weak basicity	Groups of intermediate basicity	Groups of weak basicity
DEAE-HEC-0.8[a]	0.8	31	69	8.6	6.3
DEAE-HEC-1.6	1.6	30	70	8.4	6.2
DEAE-HEC-1.9	1.9	24	76	8.2	6.0
DEAE-HEC-2.1	2.1	31	69	8.5	6.2
DEAE-HEC-2.6	2.6	36	64	8.5	6.3
DEAE-HEC-3.4	3.4	30	70	8.6	6.0

[a]Number indicates the amount of nitrogen, %

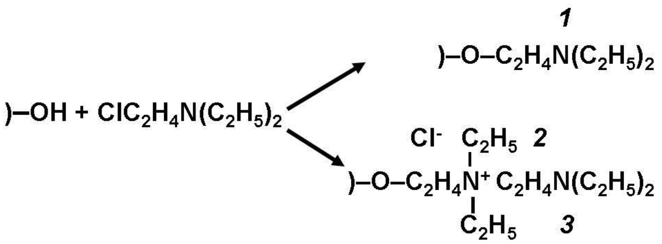

Figure 9: Reaction of cellulose with DEAE

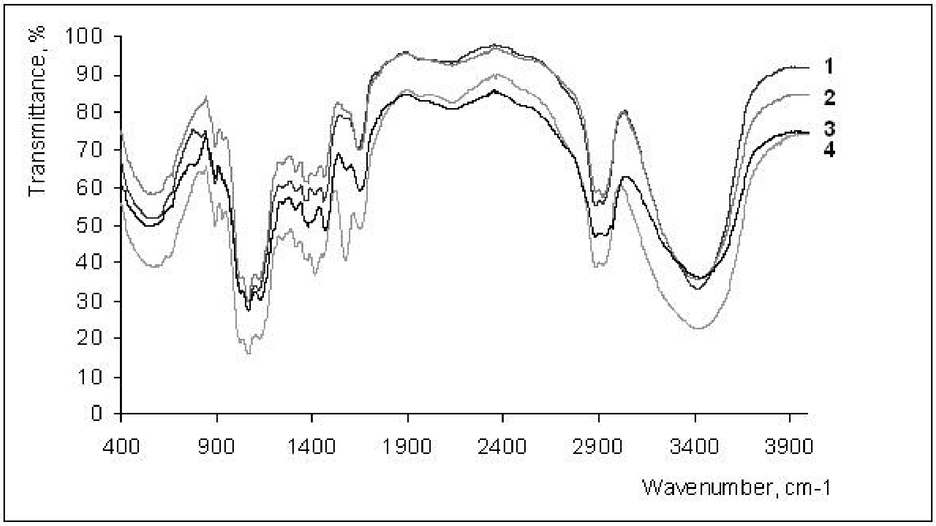

Figure 10: FT-IR spectrum of 1- DEEPA-HEC-1.2; 2- DEAE-HEC-1.2; 3- DEAE-HEC-3.6; 4- HEC

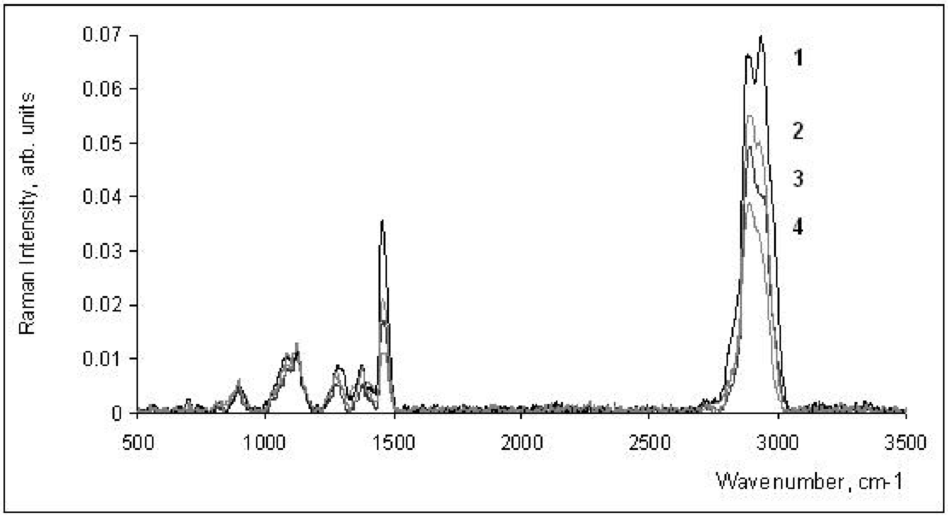

Figure 11: Raman spectrum of: 1- DEAE-HEC-3.6; 2- DEAE-HEC-1.2; 3- DEEPA-HEC-1.2; 4- HEC

The dissociation of the neighbouring amino groups 2 and 3 is hindered by each other, which results in decreasing their ionization constant. The ion-exchange capacity of cellulose derivatives at different pH depends on their ionization constant. All cationic groups of DEEPA-HEC are dissociated at a pH below about 8. In the case of DEAE-HEC, all cationic groups are protonated at a pH below about 6. At a pH ranging between 6-9, the ion-exchange capacity of DEAE-HEC is determined only by dissociation of tertiary amino groups.

Structural characterization of amino-celluloses

The cellulose derivatives were characterized regarding their structure by means of FT-IR (Fig. 10) and Raman spectroscopy (Fig. 11). With increasing the substitution degree, in the FT-IR spectrum a decrease in the intensity of the absorption bands at 3200-3500 cm^{-1} is observed, which is assigned to the hydrogen bonding vibration. Evidently, the introduced substituents reduce the possibility to form hydrogen bonds. The increase of the intensity of absorption bands at 2900-3000 and 1350-1450 cm^{-1}, characteristic of the CH, CH_2, CH_3 vibrations, reveals the successful etherification of HEC. The dependence of this increase on the substitution degree is clearly evident in the Raman spectrum (Fig. 11). It is difficult to identify unambiguously amino groups, because the absorption bands characteristic of N-C stretching vibrations are overlapped by C-H absorption. Nevertheless, a small shoulder at 2450-2650 cm^{-1} could indicate the presence of amino groups. The comparison of the intensity of the signal related to OH groups at 3418 cm^{-1} with that of the fixed peak at 1061 cm^{-1} (Table 4) reveals that, in the case of DEAE-HEC, the amount of OH groups decreases with the substitution degree. In the case of HEC amination with DEEPA, the decrease is not observed, because instead of a reacted OH group of HEC, a new OH group occurs in the substituent.

Table 4
Analysis of FT-IR spectra

Cellulose derivative	Ratio of intensity of peaks at 3418 and 1061 cm^{-1}
HEC	1.06
DEAE-HEC-1.2	0.94
DEAE-HEC-3.6	0.86

Table 5
Solubility of aminocelluloses

Cellulose derivative	Solubility					
	Water	DMSO, DMF	Acetic acid	Pyridine	1,4-Dioxane	Carbon tetrachloride
HEC	+	+	-	Sw	-	-
DEEPA-HEC-0.5	+	+	+	Sw	-	-
DEEPA-HEC-2.6	+	+	+	Sw	Sw	Sw
DEAE-HEC-1.2	+	+	+	Sw	-	-

+ Soluble, - insoluble, Sw – swells

Table 6
Cloud point of the solutions of cellulose derivatives, ^oC

pH Cellulose derivative	1	2	3	5	7	9	10	11	12
HEC	48	n.o.*	n.o.	n.o.	n.o.	n.o.	n.o.	80	-
DEEPA-HEC-2.7	70	n.o.	n.o.	n.o.	n.o.	n.o.	n.o.	n.o.	n.o.
DEAE-HEC-1.2	70	n.o.	n.o.	n.o.	n.o.	n.o.	n.o.	n.o.	n.o.

*Cloud point was not observed up to boiling temperature

Table 7
Solubility in the solutions of salts

Cellulose derivative	The highest concentration of salt, %		
	NaCl	Na_2SO_4	$Na_2S_2O_3$
HEC	30	16	32
DEEPA-HEC-2.7	10	10	23
DEAE-HEC-1.2	Up to saturation	13	32
DEAE-HEC-0.5	Up to saturation	13	32

Solubility of the aminocelluloses

The solubility of the synthesized derivatives is interesting from the theoretical and practical points of view. Knowing the solvents of the derivatives, the effect of the temperature, as well as that of the salt concentration on the solution stability, helps in choosing the proper conditions for the purification of the products and for their application. On the other hand, the solubility of the products reveals the impact of the introduced amino groups on hydrophilic-lipophilic properties of the obtained derivatives.

Due to the high polarity of the introduced substituents, the solubility behaviour of the prepared derivatives in water was the same as that of the starting polymer. The resulting derivatives are also soluble in polar aprotic organic solvents DMF and DMSO, just like HEC itself (Table 5). Moreover, the synthesized derivatives are soluble in acetic acid. Highly substituted derivatives also swell in some non-polar organic solvents, which reveals that the introduced amino groups slightly decrease the hydrophilicity of HEC. The solutions in water are stable at a high temperature in a wide range of pH (Table 6). The solution of aminated celluloses remains clear even at boiling temperature at a pH between 2 and 12, whereas the precipitation of HEC from solution is observed at pH 1 and 11 below the boiling temperature. At pH 12, HEC is not soluble at all.

HEC is famous for its tolerance for salts. However, the introduced amino groups slightly decrease the compatibility with salts, and cationic derivatives are soluble in a lower concentration of salts than HEC is (Table 7). Only DEAE-HEC demonstrated extraordinary tolerance for sodium chloride. It is soluble even in saturated solutions of NaCl.

CONCLUSION

Water-soluble aminocelluloses were synthesized by the functionalization of hydroxyethylcellulose (HEC), using two different etherification agents, diethylepoxy-propylamine (DEEPA) and (2-chlorethyl) diethylamine hydrochloride (DEAE). Comparing both methods, it may be concluded that the homogeneous etherification of HEC with DEEPA in water is one of the simplest pathways for the preparation of a cellulose-based cationic polyelectrolyte of an intermediate basicity. Since the side products of the reaction are soluble in organic solvents, the purification of the obtained cellulose derivatives is much easer than that of the derivatives obtained *via* the reaction of HEC with DEAE, where the resulting product is mixed with sodium hydroxide and sodium chloride. However, it should be mentioned that the amination agent DEEPA is not stable during long storage.

The structure of the synthesized aminocelluloses was characterized by means of elemental analysis, as well as by FT-IR and Raman spectroscopy. The composition of the cationic groups of the products was analysed using potentiometric titration. It was found that the HEC reaction with DEEPA resulted in a monofunctional cationic polyelectrolyte containing tertiary amino groups (pK_a approx. 8.2), whereas the amination of HEC with DEAE gave polyfunctional derivatives containing a mixture of weakly and intermediately basic amino groups with pK_a 6.0-6.2 and 8.2-8.6, respectively. The synthesized derivatives are soluble in polar aprotic solvents, as well as in water, and their solutions possess high stability at elevated temperature and a high concentration of salts.

ABBREVIATIONS

HEC – hydroxyethylcellulose
DEEPA – diethylepoxypropylamine
DEAE – (2-chlorethyl) diethylamine hydrochloride
DEEPA-HEC – HEC aminated with DEEPA
DEAE-HEC – HEC aminated with DEAE
DS – degree of substitution
MS – molar substitution

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