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THE NEUTRALIZATION REACTION OF NITRO-H-CARBOXYMETHYLCELLULOSE

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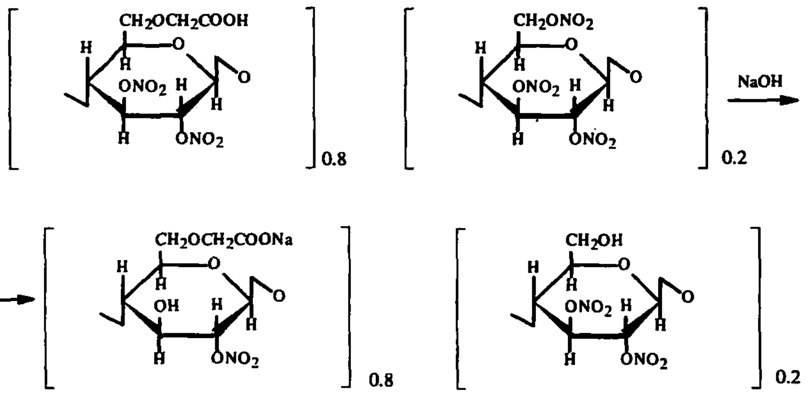
The interaction of nitro-H-carboxymethylcellulose with a solution of sodium hydroxide has been investigated. Three reactions take place in parallel: neutralization of the —COOH groups, denitration, and degradation of the main chain at the β-glucosidic bonds. Conditions permitting these reactions to be regulated have been found. It has been established that when not less than 80 mole-% of —COONa groups and not more than 130 mole-% of —ONO_2 groups are present the product of the neutralization reaction (nitro-Na-CMC) is soluble in water.

The nitration of Na-carboxymethylcellulose (Na-CMC), leading to the formation of its nitro-ester (nitro-H-CMC), has been investigated previously [1]. The deep nitration of CMC with a degree of substitution (DS) for carboxymethyl groups of 0.80 leads to the formation of a product containing 220 mole-% of nitro groups per 100 anhydroglucopyranose units. Under these condition, the substance loses its solubility in water because of the presence of —ONO_2 and —COOH groups in the macromolecule. However, nitro-H-CMC with the maximum nitrogen content is readily soluble in acetone and in a mixture of ethanol and diethyl ether.

The conversion of the COOH groups of nitro-H-CMC into —COONa groups leads to a change in the hydrophilic-lipophilic balance of the macromolecule and increases the solubility of the preparation in water at a certain content of —ONO_2 groups.

We have investigated the interaction of nitro-H-CMC with a solution of sodium hydroxide. Here, three parallel reaction take place: neutralization of —COOH, denitration with the formation of —OH groups, and degradation of the chain at the β-glucosidic bonds. The occurrence of these reactions has been shown by a combination of physicochemical methods: by IR spectroscopy, from the change in the nitrogen content, and by the decrease in the characteristic viscosity of a solution of nitro-H-CMC after the neutralization reaction.



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The neutralization reaction was performed in a homogeneous medium by adding an aqueous solution of NaOH to a solution of nitro-H-CMC in acetone or in a 1:1 mixture of ethanol and ether.

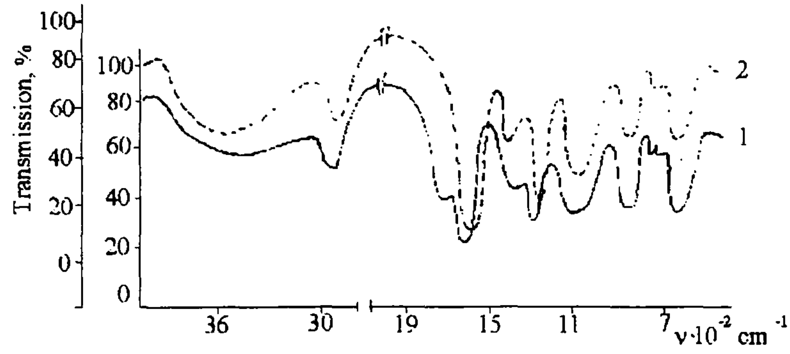

Fig. 1. IR spectra of nitro-H-CMC (*1*) and nitro-Na-CMC (*2*).

Figure 1 shows the IR spectra of nitro-H-CMC and water-soluble nitro-Na-CMC. The assignment of the absorption bands of nitro-H-CMC has been discussed previously [1]. In the frequency region of 3100—3700 cm^{-1}, the IR spectrum of nitro-Na-CMC shows a broad band relating to the stretching vibrations of the —OH groups formed on denitration. In addition, as compared with nitro-H-CMC, an absorption band at 1765 cm^{-1}, due to the carbonyl absorption of —COOH groups, had disappeared. Simultaneously, an intense absorption band due to the carbonyl absorption of —COONa groups and to the stretching vibrations of nitro groups had appeared at 1610 cm^{-1}. An absorption band was clearly observed at 1280 cm^{-1} resulting from the symmetrical stretching vibrations of nitro groups, together with other bands characteristic for them at 840, 750, and 700 cm^{-1}.

The neutralization of nitro-H-CMC was performed at various concentrations of the nitro-H-CMC solution, temperatures, and ratios of nitro-H-CMC to NaOH.

Table 1 gives the solubilities and the characteristic viscosities in water of the products of the neutralization of a solution of nitro-H-CNC in acetone with an aqueous solution of NaOH at various —COOH:NaOH ratios.

TABLE 1. Influence of the Ratio of Nitro-H-CMC to NaOH and the Time on the Neutralization Reaction in Acetone ($C_{NaOH} = 2$ N, T = 273K)

Molar ratio nitro-H-CMC:NaOH	Time of neutralization, min	N content, %	DS for NO_2 groups	Solubility in water	$[\eta]_{298K}$ in methanol-water
1:1	5	7.94	1.71	Does not dissolve	-
1:1	15	7.85	1.67	"	-
1:1	30	7.21	1.51	"	-
1:1	120	5.45	1.08	Dissolves	0.22
1:2	5	7.13	1.49	Does not dissolve	-
1:2	15	6.95	1.43	"	-
1:2	30	5.29	1.01	Dissolves	0.14
1:2	120	5.06	0.96	"	0.07
1:3	5	6.96	1.44	Does not dissolve	-
1:3	15	4.43	0.83	Dissolves	0.055
1:3	30	4.09	0.75	"	0.051
1:3	120	2.46	0.46	"	0.045

It can be seen that with an increase in the ratio the time for a reaction leading to a water-soluble product decreases. The characteristic viscosity of a solution falls sharply. When the characteristic viscosity of a solution of nitro-H-CMC measured in acetone was 3.83, after neutralization the value measured in a mixture of water and methanol had fallen to 0.22; i.e., if the degree of polymerization (DP) of nitro-H-CMC calculated by the Mark—Kuhn—Houwink equation is 411, after neutralization it has fallen to 20. This shows pronounced degradation of the macromolecule during neutralization. It must be mentioned that in all cases the characteristic viscosities of the solutions were between 0.045 and 0.22. It follows from this that the DPs, measured from viscosity indices, were between 5 and 20.

Table 2 gives the results of an investigation of the neutralization reaction in a mixture of ethyl alcohol and diethyl ether at various nitro-H-CMC:NaOH ratios and temperatures leading to water-soluble products.

TABLE 2. Influence of the Nitro-H-CMC:NaOH Ratio and the Temperature on the Neutralization Reaction in Ethyl Alcohol—Diethyl Ether (1:1, v/v) (C_{NaOH} = 0.53 N, time 2 h, temperature 273K)

Molar ratio nitro-H-CMC:NaOH	N content, %	DS for NO_2 groups	$[\eta]_{298K}$ in methanol-water
1:1.0	6.12	1.23	0.505
1:1.25	5.24	1.01	0.460
1:1.5	5.23	1.00	0.069
1:2.0	4.35	0.81	0.042
1:1.0*	6.29	1.27	0.59
1:1.25*	6.08	1.21	0.52
1:1.5*	6.02	1.18	0.083
1:2.0*	5.72	1.12	0.061

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*Temperature 298K.

When the reaction was performed in a mixture of ethanol and diethyl ether, with an increase in the NaOH content the value of [η] for a solution fell sharply, which showed degradation of the main chain of the macromolecule. As can be seen from Table 2, to impart water solubility it is sufficient simply to convert the —COOH groups into —COONa groups. In this process, denitration also takes place, this reaction being temperature-sensitive. With a rise in temperature, of course, the denitration process and the degradation of the main chain are intensified.

A comparison of the results of neutralizations of nitro-H-CMC with NaOH performed in acetone and in a mixture of ethanol and diethyl ether (Tables 1 and 2) shows that the degradation process took place far more slowly in the second case than the reaction in acetone. Consequently, the characteristic viscosities of the reaction products differed.

The different behaviors of the two solvents in the interaction of nitro-H-CMC with NaOH can be explained by their specific influences. As established previously [2], acetone behaves as a a nucleophilic reagent causing cleavage of the (1→4)-β-glycosidic bond, which leads to a decrease in the molecular mass of the macromolecule.

Table 3 shows the solubilities of samples of nitro-Na-CMC as a function of the amount of NO_2 groups in the nitro-Na-CMC molecule.

TABLE 3. Changes in the Solubility of Nitro-Na-CMC with Variations in Its Content of —NO_2 and —COONa Groups

—COONa group content, mole-%	N content, %	DS for NO_2 groups	Solubility in water
30	8.4	1.83	Does not dissolve
60	7.14	1.46	"
60	6.51	1.30	Swells
80	6.51	1.30	Dissolves
80	5.45	1.04	"
80	4.48	0.91	"
80	4.02	0.72	"

With a decrease in the $—NO_2$ group content the solubility in water increases. It was established that at a DS for $—NO_2$ of less than 0.3 with full neutralization of the —COOH groups in the molecule the product is readily soluble in water.

As can be seen from Table 3, the solubility of the samples depended on the levels of both —COONa and $—NO_2$ groups and is apparently due to the achievement of that value of the hydrophilic—hydrophobic balance of the system that permits the macromolecule to dissolve in water.

Pharmacological trials have shown that aqueous solutions of nitro-Na-CMC possess an antianginal action [3], which will permit the development of injection medicinal forms of the class of nitro drugs.

EXPERIMENTAL

In the experiments we used 2.5% solutions of nitro-H-CMC in acetone and 2.0% solutions in a mixture of diethyl ether and ethyl alcohol. The calculated amount of NaOH was added with stirring to the initial solution at 273 and 298K. The resulting precipitate was centrifuged off, washed with ethyl alcohol, and dried, and its nitrogen content was determined by the method of [4] and the degree of polymerization by viscosimetry [5]. IR spectra were taken on a Specord-75 spectrometer in KBr tablets [6].

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