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TECHNOLOGY****INVESTIGATION OF THE PROCESSES OF COMPLEXATION OF BIOLOGICALLY
ACTIVE SUBSTANCES AND SYNTHETIC POLYMERS.****U. Mirzayev¹, M. Ayupova², M. Mirzayeva³, N.G. Valeeva⁴**

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ABSTRACT

The article was studied oxadixyl complexation with water-soluble polymers - poly acrylic and polymethacrylic acid. The main methods for studying the interaction of polymers used oxadixylviscometry, potentiometry, conductivity, ultracentrifugation, ultraviolet and infrared spectroscopy. The influence of different factors on the process of complexation. Detecting that binding oxadixyl polymers leads to structing macromolecular chains of the formation of hydrogen bonds

KEYWORDS: Oxadixyl, polyacrylic acid, the extinction coefficient, polycomplex, sedimentation, polyelectrolyte, ionic strength, shielding acid groups.

I. INTRODUCTION

Use of polymers and copolymers containing -NH₂ and -COOH groups as carriers of biologically active substances (BAS) due to their good solubility in water and some polar organic media, resistance to chemical and biological agents, as well as high activity and selectivity for interaction with both charged and uncharged particles from the surfaces and, moreover, the majority of polyanions are biologically active and some of them possess bactericidal, antiviral and other types of operations [1-3].

II. MATERIALS AND METHODS

The object of investigation is selected biologically active drug oxadixyl (2-methoxy-N- (2-oxo-1,3-oxa zolidin-3-yl) acetate-2', 6'-xylidine approved MOS), code number SAN 371 F [4]. Based on the structure oxadixyl, as a carrier polymer were selected polyacrylic acid (PAK) and polymethacrylic acid (PMAK). The main methods for studying the interaction of polymers used oksadixilomviscometry, potentiometry, conductivity, calorimetry, ultracentrifugation, dialysis, UV spectroscopy, IR spectroscopy.

III. RESULTS AND DISCUSSION

Some information about the changes in the structure of organic matter in the binding process can be obtained by studying the structure polycomplexes by IR and UV spectroscopy. The interaction of organic molecules to the polymer chain changes the distribution of the electron density in the molecule, which is reflected in the IR spectra of their complexes. Analyzing the results, one can draw the following conclusions about the structure of the compounds obtained. Increasing the intensity of the absorption band of 1660-1710 cm⁻¹, the appearance of a broad intense absorption band 3300-3500 cm⁻¹ and a shoulder at 2350 cm⁻¹, all confirms the possibility of the formation of hydrogen bonds between the carboxyl and hydroxyl oxadixyl carboxyl groups of PAK and PMAK. In addition, new absorption bands 760, 910, 1010, 1270 cm⁻¹, characteristic oxadixyl.

On the possible influence of the media on the structure of the polymer binder can be judged according to UV spectroscopy. Regulation oxadixyl solution and polymer complex (at the same concentration oxadixyl) at 256 nm it remains, but there is a reduction in the absorption intensity in the complex.

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In the literature [4-5] that carboxyl polymers unlike other ionic polymers characterized by a "soft" interaction with a binding organic substance that does not lead to significant deformations of the chemical structure.

Increasing the amount of organic matter associated effect on the value of the apparent molar extinction coefficient (ϵ), which enables the use of UV spectroscopy for the impact of certain quantitative patterns (Figure 1)

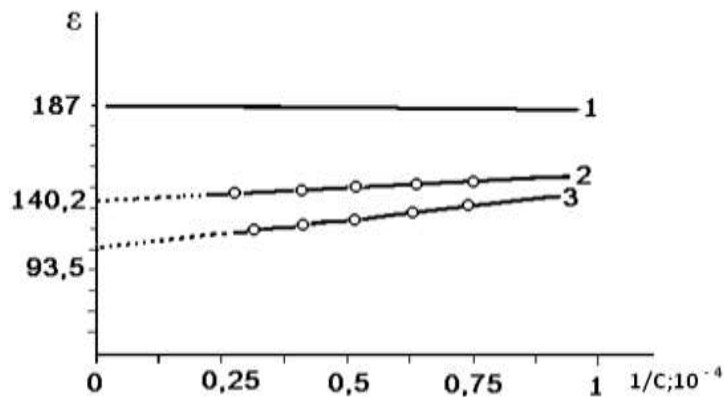


Fig.1. Dependence molar extinction oxadixyl(1). A solution of the polymeric complex PAK + oxadixyl (2) and PMAK + oxadixyl (3)

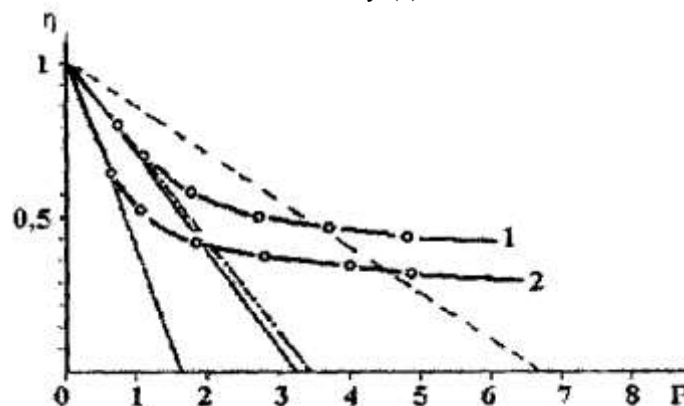


Fig.2. The dependence of the share of unbound molecules oxadixyl his polycomplexes with PMAK (1) and PAC (2). $P = [\text{polymer} / \text{oxadixyl}]$.

From 1 that the apparent extinction coefficient slightly decreases with increasing concentration of biologically active substances. According to Schwartz decrease extinction coefficient polymer complexes is due to the increase in the proportion of the associated biologically active substances and redistribution of the electron density of the chromophore groups in the binding polymer. The trend towards a decrease in the apparent extinction coefficient with increasing concentration of the polymer complex indicates an increase in the proportion of the associated biologically active substances in the limit, when extrapolating this dependence to an infinitely high concentration of biologically active substances can be determined extinction coefficient related molecules in BAS saturated complex (ϵ). If the extinction coefficient of unbound molecules designated as (ϵ), the following formula:

$$\gamma = (\epsilon - \epsilon) / (\epsilon_{oks} - \epsilon)$$

where: γ - proportion of unbound molecules BAS with different ratios of polymer / biologically active substances, but at a constant total concentration in the solution can determine the proportion of unbound molecules BAS.

According to the theory of Schwartz extrapolation of the initial part of the curve γ P axle P enables us to determine the number of units of the polymer that binds a single molecule of BAS (n) in the saturated complex (Figure 2, dashed line). The second line, which has twice the slope of less intersects the curve at the point γ .

According to the theory, the importance of the impact of γ' -unbound fraction of biologically active substances in a saturated complex allows to calculate the binding constant of $K = \gamma / \text{BAS}$ and cooperative process parameter g in next formula.

$$g = n \cdot P(1 - \sqrt{\gamma}) / \gamma$$

The calculated kinetic parameters of the binding of PMAK and PAK with oxadixyl given in Table 1.

Kinetic parameters of the binding of the PAC and PMAK with oxadixyl

Complex	γ'	$K \cdot 10^{-5}$	n	g
PAK-oxadixyl	3,5	2,266	1,7	3,1-53,4
PMAK-oxadixyl	6,6	4,4	3,3	12,0-34,2

Education polycomplexes can be confirmed, and by sedimentation velocity by determining the sedimentation coefficient (S) of the starting polymer and its complexes with oxadixyl.

Research sedimentation constant depending on the composition of his political systems confirms the presented model of interaction PAK, PMAK with oxadixyl. The results of sedimentation velocity of mixtures of components in the composition QA / Paul. = 0 - 2.5 indicating the formation of soluble complexes. On sedimentogram mixtures of PAK, PMAK with oxadixyl, there is a single peak corresponding to the complex particles. Sedimentation coefficient peak PAC without additives oxadixyl characterized by S complexes that show a significant impact on the state of organic molecules in the PAK solution. Figure 3 shows the dependence of S on the composition of the mixture of PAK+ oxadixyl.

As can be seen from the figure for the values of QA / PAK = 0.1 sedimentation coefficient complexes increases sharply, indicating that the binding oxadixyl with PAK, leading to an increase in the sedimentation coefficient. Further increase oxadixyl not affect the sedimentation coefficient of a macromolecule. The hydrophobic interaction between PAK and oxadixyl greatly changes the dependence of S on the initial ratio of components.

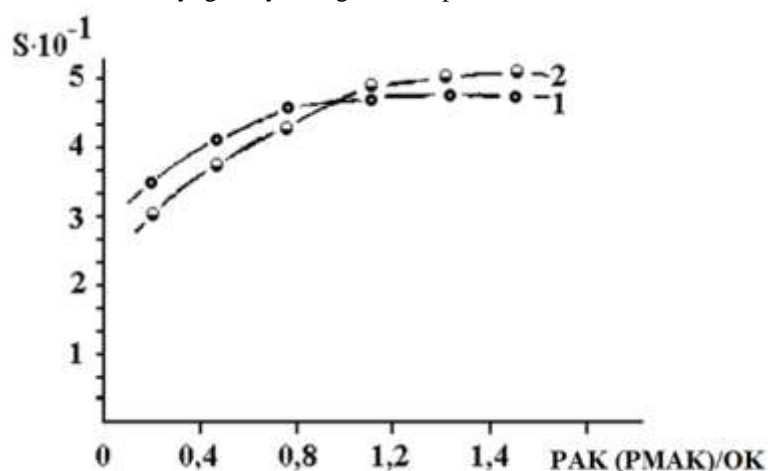


Figure 3. The dependence of the sedimentation coefficient of mixtures of PAK (1), PMAK (2) the relative concentration oxadixyl

Adding a small amount oxadixyl increases sedimentation coefficient of macromolecules, as a consequence of hydrogen bonding increases with increasing hydrophobic interactions and the influence on the process of binding, whereby as already mentioned is formed polycomplex soluble at all ratios.

At the depth and the stability of complexation of the resulting products is influenced by various factors: the length of reacting chains, their flexibility, the conformation of the polymer chain microstructure, and properties

of the medium (component concentration and their degree of ionization, the temperature and solvent composition, pH of the medium).

It is known that the conformation of PMAK and PAK chains in aqueous solution in a non-ionized state differ greatly. This is due to the presence of the structured state α -methyl groups together. It can be expected that the compact conformation of macromolecules PMAK should affect its interaction with various substances. Thus, we have shown high stability of polymer-polymer complexes, one component of which \rightarrow PMAK.

An interesting question about the nature of the interaction in these systems. A low degree of ionization of the carboxyl groups of polyacids and very weak in basicity of tertiary nitrogen oxadixyl (OK), apparently eliminates electrostatic attraction between them. The reduced viscosity of the polymer compounds OK on dilution falls, which is typical of non-ionic macromolecular substances, whereas PAK and PMAK behave like regular polyelectrolyte. Obviously for weakpolyacids can assume interaction with UC through hydrogen bonds by the hydroxyl and carboxyl groups. In this case, the shielding of the acid groups will lead to a decrease in hydrogen ion concentration and therefore to an increase in pH (Figure 4, curve 3). The different character of the curves η_{sp} / C - a composition for polymer compounds OK with PMAK and PAK can probably be explained by the peculiarities of the conformational state of the polymers used.

The presence in the molecule or BAS various functional groups facilitates the formation of multiple types of bonds, the proportion of which vary depending on the composition and the reaction conditions. Thus, the interaction was investigated with kanamycin copolymer of vinyl alcohol and vinilamidoyantarnoy acid and found that the binding of the drug characterized by cooperativity, i.e. dependence of the number of binding kanamycin on the degree of "filling in" macromolecular polymer carrier molecules of the drug.

At low BAS concentrations realized interaction between hydroxyl and carboxyl groups of two carboxyl groupsoxadixyl. As a result of the macromolecule polymer becomes more compact, so that the observed decrease in the viscosity, but a further increase in the concentration of oxadixyl leads to a slight increase in viscosity, probably by increasing the size of the macromolecule polymer.

It is known that with an increase in temperature, or the use of organic solvents, are competitors for hydrogen bonding occurs weakening and destruction of the latter. Investigation of thermal stability OK-PAK found that increasing temperature leads to the appearance of abnormal reduced viscosity depending on the concentration, i.e. OK destroyed complex PAK and polyelectrolyte solution appears unrelated. OK polymeric compound with PAK characterized great strength to thermal influence - temperature rise to 70 ° C does not affect the stability of the complexes (Table 2).

Table 2

The intrinsic viscosity $[\eta]$ complex oxadixyl with PAKPMAK and when changing the temperature and ionic strength

PAK - oxadixyl				PMAK - oxadixyl			
T°C	$[\eta]$	μ	$[\eta]$	T°C	$[\eta]$	μ	$[\eta]$
20	0,48	0,0	0,48	20	0,46	0,0	0,46
25	0,43	0,01	0,39	25	0,52	0,01	0,52
35	0,34	0,05	0,26	35	0,38	0,05	0,38
45	0,38	0,1	0,44	45	0,31	0,1	0,31
55	0,51	0,2	0,43	55	0,42	0,2	0,42
75	0,44	0,3	0,10	75	0,44	0,3	0,44

Since the only difference between TAP and PAK is present in the PMAK lateral methyl groups, we can

assume a significant role of hydrophobic interactions in contact with PMAK OK. In organic solvents, as it is known, not only destroys H bond, but also weaken hydrophobic interactions.

The stability of the polymer compounds to the action of dimethyl sulfoxide OK. On Figure 5, the dependence of the relative viscosity (viscosity of the solution mixes OK - PAK (PMAK), divided by the viscosity of polyacids) the composition of the mixed N₂O + DMSO-acetone. In the case of polymeric compounds QA-PACK a monotonic increase in the size of macromolecules in the enrichment of the mixture with dimethyl sulfoxide (curve 2). Curve η_{rel} (OK-PMAK) - compound solvent seen at least that OK in the PMAK-adding an organic solvent is first noticeable decrease in the size of macromolecules, and only then their growth (curve 3).

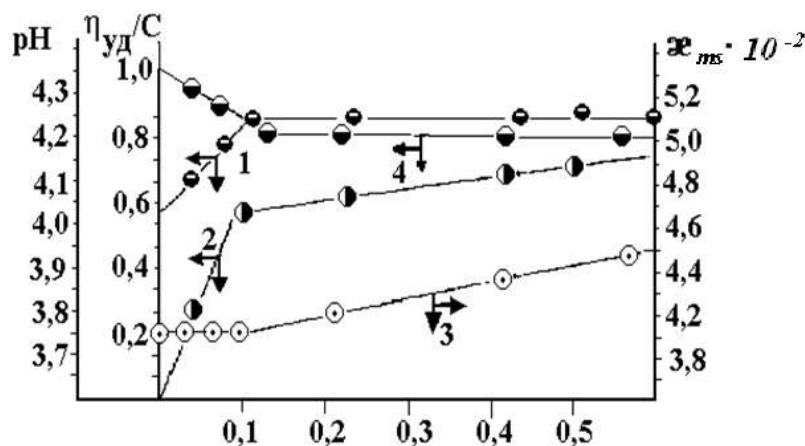


Figure 4. Changing the reduced viscosity (1,4), pH (2) and electrical conductivity (3) PAK complexes - oxadixyl (1,2,3) PMAK + oxadixyl (4)

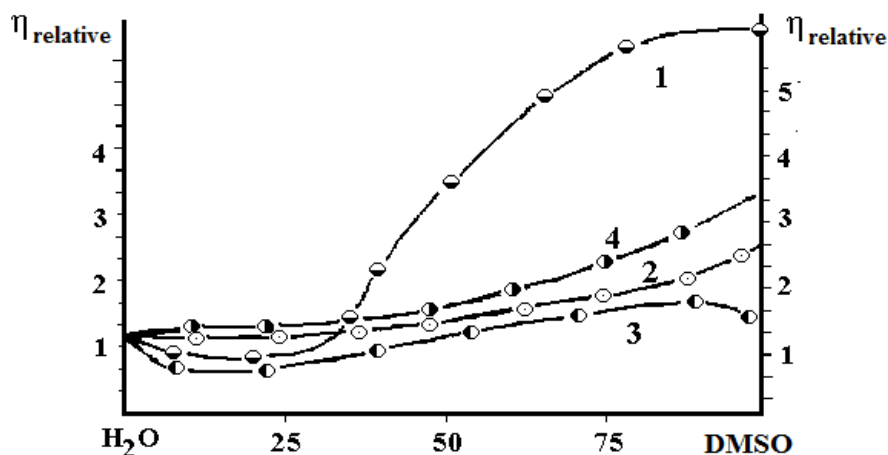


Figure 5. Influence of solvent composition H₂O - DMSO at a relative viscosity of PMAK (1), PAK - oxadixyl (2) and PMAK - oxadixyl depending on the ratio of the components

This dependence is typical for macromolecules free PMAK (curve 1). The fall of viscosity, probably due to rearrangement of the resulting structures and change in the interaction between them, and a solvent. The character of the curves η_{rel} - composition of the mixed solvent systems studied indicates a role of hydrophobic interactions in the formation of polymeric compounds PMAK with OK.

IV. CONCLUSION

Thus, the binding of PAK and OK with PMAK leads to structure of macromolecular chains due to the formation of hydrogen bonds between the functional groups of both components and hydrophobic interactions.

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