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POLYMER COMPLEXES IN VETERINARY PHARMACOLOGY

Summary. *The results of studies on the synthesis of polymer complexes of antiprotozoal substances used in veterinary practice and the creation on their basis of drugs with specific activity, low toxicity, mild and prolonged action are presented. It is shown that the achieved pharmacological properties are based on the use of polymeric materials in the developed dosage forms. It has been established that during the immobilization of low molecular weight compounds, the "polymer effect" appears on macromolecules.*

The last decades of the 20th century were crowned with many introductions into pharmacological practice of scientific research and development of polymer chemistry [1]. This, in turn, provided the basis for the emergence of drugs with a targeted action due to the polymer shell, therapeutic systems with several directions of physiological activity, due to the application of several layers or substrates of polymers, as well as drugs with the property of a "polymer effect", which low molecular weight organic compounds cannot possess [2]. At the same time, requirements and principles for the selection of macromolecular compounds, especially synthetic polymers, were formulated, depending on the field of application, form of administration, pharmacological properties, and chemical structure of physiologically active compounds. It should be noted that in this area of science, the contribution of scientists of our Republic was significant, and in the creation of veterinary drugs, the development of the "scientific school" created by Doctor of Chemical Sciences, Professor, Honored Scientist of Uzbekistan U.N. Musaev has a special place [3, 4]. Based on the complex physicochemical, pharmacological and pharmacokinetic studies carried out in 1990, the drug "POLYAMIDIN" was introduced into veterinary practice, which has a wide antiprotozoal spectrum of action, low toxicity and prolonged action, which is a complex of 3,3-bis (2-imidazoline -2)-carbanemide with polymethacrylic acid.

Currently, at the Department of Polymer Chemistry of the National University of Uzbekistan named after. M. Ulugbek, new veterinary drugs are being developed: gynecological "CARBOKAZ" and biologically active additives based on natural and synthetic polymeric substrates. Since the objects of our research were the preparations imidocarb and azidine, which, when dissolved in water, form positively charged organic ions, synthetic polymers containing

carboxyl groups were taken for their immobilization. In order to localize the main amount of the drug at the injection site and to exclude the biotransformation of the carrier polymer from the injection site, one of the requirements was a sufficiently large molecular weight of the carrier polymer macromolecules ($M_n \geq 200000$), at the same time to achieve a sufficiently high concentration per unit volume of the dosage form, they must have good water solubility.

The developed dosage forms, having the same therapeutic dose as the original drugs, have lower toxicity, prolonged time of physiological activity, and, which is especially important in the weakened state of diseased animals, mildness of action.

By studying the process of interaction of aqueous solutions of initial preparations with synthetic polymers by various methods, it has been established that ion-ion and hydrogen bonds, as well as hydrophobic-hydrophilic interactions, are realized in the process of their immobilization on macromolecules. Using the methods of high-speed sedimentation (ultracentrifugation) and visually at high initial concentrations of components, the dynamic nature of the immobilization of low molecular weight molecules on macrochains was established, which is manifested by the establishment of an equilibrium state in the organic substance/polymer system after a certain period of time.

The results of pharmacological studies of the antiprotozoal drug "CARBOKAZ", which is a complex of imidocarb with Na-carboxymethylcellulose, showed that LD₅₀ for white mice is 600 (360±840) mg/kg, for white rats - 375 (280±475) mg/kg when administered subcutaneously. administered. In experiments in which the chronic toxicity of the drug was studied at doses of 5 and 20 mg/kg in rats, and in dogs at doses of 2 and 10 mg/kg, after 10 injections, no changes in the behavior of animals were found.

The complex formation of synthetic polymers with metal ions is a modern way of delivering macro- and microelements to a living organism, which are necessary for the development, maintenance, and restoration of cells and tissues [5]. Currently, we are conducting research on the synthesis of polymer complexes based on polypeptides obtained by alkaline hydrolysis of the *Bombux Mori* silkworm, an available natural raw material in Uzbekistan. The ongoing work is aimed at studying the mechanism and features of the complex formation of these polypeptides with microelements using modern physical methods for studying macromolecular compounds in order to correct the balance of microelements in a living organism, modeling the processes occurring in it [6, 7]. Comparison of the hydrodynamic and dynamo-optical characteristics of metal-polymer complexes with polypeptides of various compositions and molecular weights made it possible to estimate the degree of binding and conformation of macromolecules of these polymers in aqueous solutions [8, 9]. After hydrolysis, the fiber was washed with distilled water several times until a neutral medium (pH 6.0-6.5), after which the fiber was placed in 50 ml solutions of 0.1 N calcium chloride, magnesium sulfate, zinc sulfate (CaCl_2 ; $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$; $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$). The formation of metal-polymer complexes was confirmed by IR spectroscopy.

The study of the effect of the introduction of the obtained metal chelate complexes on the biochemical parameters of the blood revealed the absence of significant changes. In an *in vitro* study, the effect of the drug administration on the functions of the liver, kidneys, spleen, stomach, intestines, heart and injection site, as well as on the orientation reaction, hypnotic effect, anticonvulsant and curare-like properties, pressure and respiration, showed minor changes, which gives reason to attribute this preparation belongs to the 3rd class of harmless substances according to GOST 12.1.007.

The results of the comprehensive studies carried out became the basis for the preparation of technical conditions, instructions and production regulations for the production of new drugs: "POLYCARB" and "CARBOKAZ".

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