Die Ergebnisse der Festigkeitseigenschaften und die Daten über Porenvolumengesamtzahl sind auf den Abb. 1-2 dargestellt. Bruchhärte bei statischen Bedingungen wurde mit dem konischen Plastometr mit dem Kegelwinkel 60° gemessen. Das Porengesamtvolumen wurde mit Hilfe der Adsorption von Benzoldämpfen bestimmt (Abb. 2).

Bei Pulvertablettierung mit 0,1 % von PAA-, CMC- und MC-Lösungen kann man sehen, dass die zunehmende Konzentration der Bindeflüssigkeit die Kornfestigkeit erhöht. Da das Bindemittel in der wässrigen Phase gelöst ist, wird sie bei der Trocknung der Tabletten entfernt. PAA, CMC und MC werden in die feste Substanz verwandelt, die die Pulverteilchen mit einander verbindet. Aus der Abb. 1 ist es klar, dass der erhöhte Gehalt von Bindemittel die Tablettenfestigkeit von 40 bis 70 %. erhöht.

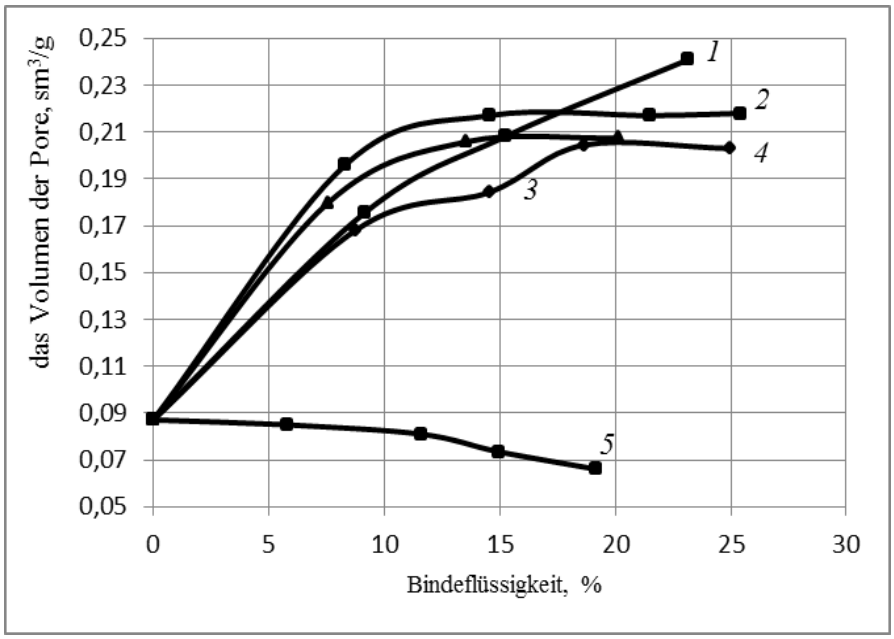

Abb. 2. Abhängigkeit des Porenvolumens vom Bindemittel: 1 – 0,1% PAA, 2 –1% Glyoxal, 3 – 0,1% MC, 4 – 0,1% CMC, 5 – Glycerin.

Untersucht werden die physikalisch-chemischen Eigenschaften des Pulvers, und auch Tabletten – Sorptionsmittel: Fließfähigkeit, Wasseraufnahme, Benetzbarkeit, Korngrößenverteilung, die wahre, die relative und Bulk-Dichte, прессуемость,die Haltbarkeit auf Brüche und das Volumen der Pore. Korngrösse oder Verteilung der Partikel des Pulvers nach

Die Verwendung von Glycerin und 1 % Glyoxal führt zu einer deutlichen Verringerung der Tablettenfestigkeit, und je mehr Bindemittel enthält die Masse, desto ungefestigter sind die Tabletten. Es ist damit verbunden, dass Glycerin und Glyoxal in der Tablette in Form einer flüssigen Phase sind und flüssige Brücken bilden, die sich mit der Zeit nicht in die feste Phase übergehen. Deshalb erhöht Glycerin in der Tablette auch die Zahl der flüssigen Brücken und verhindert die Verhärtung der Tablette, sowie führt zu Verringerung des Porenvolumens.

Die Zunahme des Porenvolumens bei den anderen Bindeflüssigkeiten ist damit erklärbar, dass bei der Trocknung die Polymerisation des Bindemittels passiert, was zur Bildung der zusätzlichen Poren führt. Obwohl die Tablettierung mit Glyoxal zur Erhöhung des Porenvolumens führt, sinkt aber die Festigkeit der Tabletten.

Zusammenfassend kann man sagen, dass die effektivste Bindeflüssigkeit für die Tablettenfestigkeit 0,1 % PAA ist. Als Bindemittel für die Ausfalltablettierung kann man auch 0,1 % CMC und 0,1 % MC empfehlen.

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INDIRECT ELECTROCHEMICAL DETERMINATION OF HEPARIN IN PHARMACEUTICALS

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Heparin is a complex, highly negatively charged polysaccharide, which consists of repeating disaccharide units of iduronic/glucuronic acid and glucosamine residues. It was the second major biopolymeric drug introduced into

medical practice more than half a century ago (after insulin) [7]. Heparin can be found in blood vessels, liver capsules, lungs, skin, intestines, and the peritoneal walls; it performs anticoagulant, antithrombotic, antilipemia, and antiatherosclerosis functions [4]. Monitoring heparin in blood and other biological fluids is an important problem during surgery and the immediate postsurgery period, still waiting for adequate solution. The methods for determination of heparin can be classified by biological and chemical features. The application of biological methods is limited because it is greatly affected by biological individuals and cannot be easily mastered, performed and interpreted [8]. Currently, the following chemical methods for heparin determination are known: spectrophotometric [5, 10], spectrofluorimetric [3], high performance liquid chromatography [6], electrochemical [13, 11], piezoelectric quartz crystal sensor [12], capillary electrophoresis [9], resonance light scattering imaging [2], biochemical methods [1], etc.

In this paper cationic malachite green (MG) dye was used for determination of heparin in pharmaceuticals by constant-current sweep voltammetry on the mercury-film electrode. It is capable of forming a complex with heparin. The presentation of optimized methodology of voltammetric heparin determination in simple electrolytes is the main purpose of this paper.

Heparin sources for the study were a pharmacological solution of high heparin sodium in the form of the tetrasodium salt (Na_4Hep), for internal and subcutaneous administration, production "Moscow Endocrine Plant" - each milliliter of this solution contains 5000 units and Fraxiparine (low molecular weight heparin) Glaxo Wellcome Production, France (9500 units in 1 ml).

The electrochemical studies were carried out at the voltammetric analyzer TA -2 ("Tomanalyt", Tomsk production) with a three-electrode system including the indicator mercury film electrode, a silver chloride reference electrode, and a platinum auxiliary electrode. The MG dye solution with the classification “pure for analysis” was prepared by dissolving 0.1825±0.0002 g of its sample in 50 ml of distilled water. The standard titer of 0.05 M potassium tetroxalate dehydrate ($KH_3C_4O_8 \cdot 2H_2O$) with pH 1.65 was selected as a background electrolyte. The electrochemical properties of heparin depending on influence of various factors, such as the nature of background solution, pH, an electrode material, potentials and accumulation time on an electrode were investigated. Taking into consideration the above factors, heparin analytical signal was not detected. Therefore, further research of the electrochemical properties of heparin was carried out in complex with MG dye. Hence, the research of the MG electrochemical properties became the initial stage in this work.

The electrochemical behavior of MG was investigated by the methods of cyclic and cathodic voltammetry with constant-current potential sweep on MFE. During the research it was observed that MG on MFE is electrochemically active only in the cathodic area. The study of the pH effect on the electroreduction peak of MG showed that the current reaches its maximum at pH = 1.65. Moreover, in this work light impact on a signal from dye was investigated, as a result of which it was stated that the signal of electroreduction of the MG in the light has twice low intensity than the signal from the MG solution which has been in the dark. On the basis of this all subsequent studies with the MG were carried out in the dark conditions at pH=1.65. Having picked up the conditions for receiving the stable and reproduced signal from MG, the following stage in work became the research of electrochemical properties of MG in a complex with heparin.

The electrochemical research of MG in complex with heparin was studied on MFE by cathodic voltammetry with constant-current potential sweep (W = 80 mV/s) in potential range from 0.0 V to -1.2 V. In the 0.05 M potassium tetraoxalate buffer solution with pH 1.65 MG had a well-defined peak of electroreduction at - 0.46 V. In the study of the electrochemical properties of MG in complex with heparin, in addition to the signal from the dye at E=-0.46 V, the second signal at E=-0.87 V was found. Increasing the concentration of heparin in the solution led to decrease of signal intensity at E=-0.87 V (Figure).

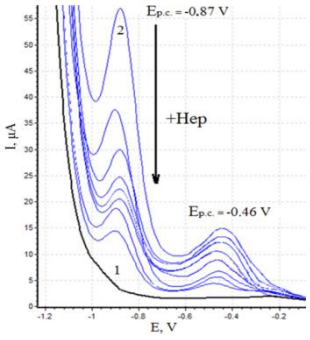

Fig. Voltammograms of reduction of complex MG-Hep depending on the concentration of heparin in the cell. 1 - background curve; 2 – $1.0 \cdot 10^{-3}$ mol/dm^3 malachite green with heparin sodium in volume from $3.9 \cdot 10^{-4}$ mg/ml to3.9 10^{-3} mg/ml. W = 80 mV/s, pH 1.65

The optimum conditions for the electrochemical determination of heparin in dosage form using malachite green were picked up. Influence of auxiliary components of the heparin dosage form on the electroreduction of the complex malachite green-heparin (MG-Hep) was investigated. The area of rectilinear dependence was kept in the range of heparin concentration (taking into account the activity of a medicinal form) from $3.9 \cdot 10^{-4}$ mg/ml to $3.9 \cdot 10^{-3}$ mg/ml.

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