Section 2. Chemistry

DEVELOPMENT OF IONOSELECTIVE ELECTRODES FOR RAPID DETECTION OF DRUGS BASED ON DODECOMOLIBDOPHOSPHATE IONOPHORES

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Abstract

Ion-selective electrodes with a plasticized membrane based on dodecomolibdophosphate acid were developed for the express analysis of ori products. The main electrochemical parameters of the developed ISE: the linear range of the signal (of the electrode function), the slope of the electrode function, the lowest limit of ion detection, etc.determined.

Keywords: *Medicines, ionometric method, ion selective electrode, ionophore compound dodecomolybdophosphate acid, dibazol, pyridoxine*

Introduction

In the world, much attention is paid to the control of the production and composition of medicinal substances. In this direction, certain fundamental and practical results have been achieved in Uzbekistan. In the republic, much attention is being paid to the further reform of the healthcare sector, first of all, to reducing the level of morbidity and increasing the life expectancy of the population (Decree of the President of the Republic of Uzbekistan, Decree No. PF-5590 of 07.12.2018).

In this direction, it is urgent to rapidly develop methods of monitoring the composition of pharmaceutical products and the technological processes of their production, to develop modern operational methods of analyzing the composition of products, and to create high-performance sensors that solve various problems based on them.

Ionometric method of determination of drugs is one of the most common methods. Instruments based on this method (ionomers) are available in almost every laboratory, so information about ionometric methods

of determination of various medicinal substances is of particular importance.

Potentiometry based on the use of an ion-selective electrode is an alternative to time-consuming and expensive methods such as high-performance liquid chromatography, capillary electrophoresis and spectral analysis due to the simplicity and speed of the equipment in the analysis conditions (Matveychuk, Yu.V., 2016; Matveychuk, Yu.V., 2017). Therefore, one of the important tasks of analytical chemistry is to create and research new high-performance ISE based on existing electrode active substances for drug analysis. Such electroactive substances include dodecomolybdophosphate heteropolyacids (GPK) and their derivatives, which are significantly superior to natural ionophores in terms of selectivity and sensitivity (Ceresa A., Sokalski T., Pretsch E., 2001; Smirnova A. L., Khitrova V. L., Shvake A., 2000; Kharitonov S. V., 2001).

The purpose of this work development of membrane ion-selective electrodes based on dodecomolybdophosphoric acid (DDMF) for rapid analysis of medicinal substances and testing their indicators. In order to achieve the goal set in the work, the synthesis of soluble electrode-active compounds based on drugs with DDMF was carried out.

The technology of obtaining plasticized membranes with the resulting ionophores was developed, researches were conducted in the field of establishing the effect of the composition of the drug-detecting ISE membrane on its indicators.

Methodology and materials

Dodecaphosphomolybdate acid and medicinal preparations as an electrode-active substance (ionophore) in work: dibazol and pyridoxinecompounds obtained on the basis of

Synthesis of ionophores was carried out at room temperature (25 °C). Aqueous solutions of relevant drugs (dibazole and pyridoxine) were added to aqueous solutions of dodecophosphomolybdate heteropolyacid (GPK) heated to 25^0C with constant stirring. After some time, a white precipitate will settle. The precipitate was then separated from the liquid, washed with cold distilled water and dried for one day. Taking into account the tribasicity of dodecaphosphomolybdate acid and the possibility of protonation of three molecules of dibazole, the molar ratio of GPK and dibazole was taken as 1:3, respectively.

The table shows the results of the synthesis of ion associates based on DDFM and pyridoxine and dibazole drugs.

Table 1. *Results of synthesis of ionophores based on dodecaphosphomolybdate acid and drugs (pyridoxine, dibazole)*

	Gross formula of EAS	Initial salt	Color of EAS	Product yield,%	Solubility of obtained EAC
	Starting component – 25 ml of 0.01 M $H_3[R(Mo_3O_{10})_4]2H_2O$ solution				
1	$(Pyridoc)_3[R(Mo_3O_{10})_4]2H_2O$	pyridHCl	Light green	96.7	Low solubility
2	$(Dib)_3[R(Mo_3O_{10})_4]2H_2O$	DibHCl	Dark green	90.5	Low solubility

ISE plasticized film membranes were prepared by dissolving PVCH, dioctyl phthalate plasticizer, and electrode active compound (EAC) in tetrahydrofuran with constant stirring. The EAC content was 1–5% by weight of the membrane; The ratio of PVC-plasticizer was 1:2 by weight. The electrode consisted of a cylindrical Teflon body with a plasticized membrane attached to its tip. ~1.5 mL of internal reference solution containing potential-determining ion $(1·10^{-5}–1·10^{-4}$ M) and 1–2 drops of 3M KCl was introduced into the electrode body. A silver wire covered with a layer of silver chloride was taken as an internal reference electrode.

The obtained results and their discussion

Inspection of pointers and electrode calibration of ISE developed on the basis of dodecaphosphomolybdate acid and drug was carried out in the following order. Before measuring the potential, the electrodes were prepared in the prescribed manner. Tests were carried out on the example of ion-selective electrodes (dib.-DDFM, pyridok.-DDFM)

prepared using ionophores developed on the basis of drugs (Dibazol and pyridoxine hydrochloride) and dodecaphosphornomolybdate acid. The electrode potential was determined by measuring the EC of the investigated electrode system in accordance with the state standard 8.213–76 at a temperature of 25 ^{0}C, using dibazole and pyridoxine hydrochloride solutions with a concentration of 10^{-2} mol/l.

The dependence of the signal value of the developed electrodes for detecting different drugs on the concentration of the detected substance in the solution was studied in the concentration range of $10^{-1}–10^{-7}$ mol/l. The results of this experiment are presented in (Table 2).

Table 2. *Dependence of the signal of ISEs developed on the basis of dodecomolybdophosphate on the concentration of the detectable drug in the solution (n=5, r=0.95)*

Ion concentration, mol/l	Drug matching signal of ISE, mV					
	Dibazol hydrochloride			Pyridoxine hydrochloride		
	x ± Δx	S	Sr*10²	x ± Δx	S	Sr*10²
10^{-1}	277.2±1.8	1.45	0.52	229.1±2.2	1.77	0.77
10^{-2}	232.1±1.9	1.53	0.66	171.1±1.7	1.37	0.8
10^{-3}	184.3±1.6	1.29	0.7	115.2±1.8	1.45	1.26
10^{-4}	138.4±1.4	1.13	0.81	60.2±0.7	0.56	0.93
10^{-5}	95.0±1.0	0.8	0.85	34.3±0.2	0.16	0.47
10^{-6}	72.3±1.1	0.88	1.22	15.4±0.4	0.32	2.09
10^{-7}	63.2±1.1	0.88	1.40	11.5±0.1	1.77	0.77

The main electrochemical parameters of any ISE include parameters such as the linear range of the signal (of the electrode function), the slope of the electrode function, the lowest limit of ion detection, the selectivity coefficient, and the dynamics of the electrode signal (response time). All parameters of the signal, except dynamics, are determined from the expression E-pA, the dependence of the electrode potential on pA. Using the indicators of the ISE, a conclusion is made about the performance of the electrode. The main characteristic of the measuring electrode is the range of performance of the electrode function (Nernst equation) — this is the part of the range of the concentration dependence of the signal in the range of ion detection, which has a straight line. Based on the results of determining the performance interval of the Nernst region of the membrane electrode developed on the basis of dodecophosphomolybdate and the corresponding drug, it was shown that the developed electrodes have the ability to detect drugs in the concentration ranges of $10^{-1}–10^{-5}$ mol/l, depending on the ionophore content. It was observed that the highest detection range of the studied ISEs corresponds to the ISE developed based on pyridoxine and DDFM. The results of determining the electrode function of this electrode are presented in (Figure 1), and we can see that the developed electrode has the ability to detect pyridoxine in the concentration ranges from 10^{-1} mol/l to 10^{-5} mol/l, depending on the ionophore content.

Another indicator of a drug-selective electrode is the slope of its electrode function (K), which is:

$$K=X/U$$

is found by Eq. In this case, X = ΔE and U = Δp A.

According to the Nernct coefficient, the theoretically calculated value is 58 mV for singly charged ions and 29 mV for doubly charged ions.

Slope percentage of electrode function:

$$A\%= K/58 \cdot 100$$

is determined by Eq., and this indicator is used to determine if the electrode is working properly. From the results of determining the slope of the electrode function of the ISE developed on the basis of EAC containing Dibazole-DDFMK (Figure 2), the value of K was analyzed: K= ΔE/ΔpA=231/4.11=56.2 a and

the percentage of the slope = (56.2/58)100 = =96.9%. The results of the study of the slope of the electrode function for the electrodes developed on the basis of membranes with different compositions are presented in (Table 3).

Figure 1. *Performance interval of the electrode function of the ISE developed on the basis of Pyridox-DDFMK, which identifies the drug pyridoxine*
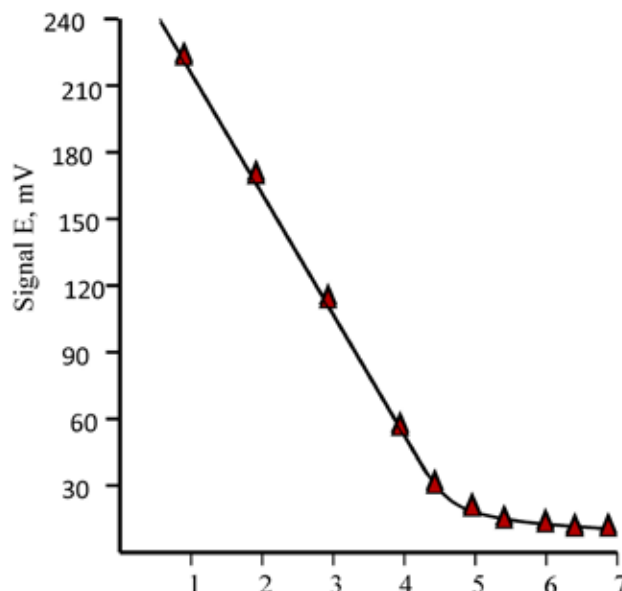

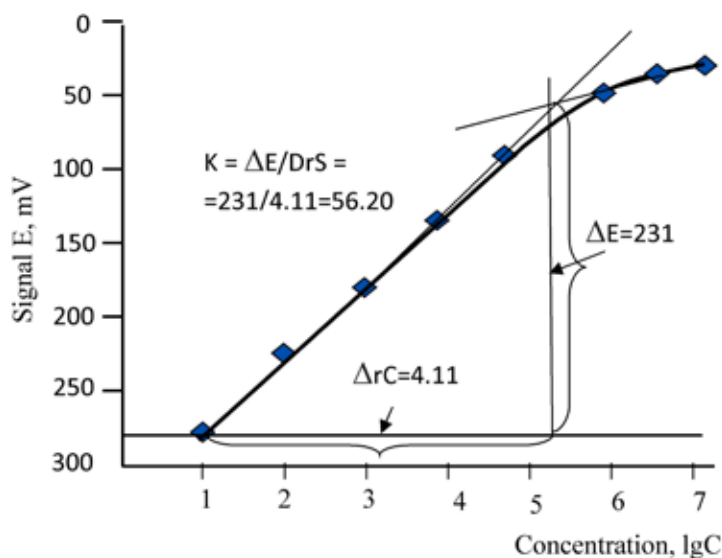**Figure 2.** *The slope of the electrode function of ISE developed on the basis of EAB containing Dibazole-DDFMK*

Table 3. *Values of the slope magnitude of the electrode function corresponding to the respective ions of the developed ISEs (n=5, P=0.95, Cion = 10−2 mol/l)*

| t/r	The composition of the ionophore	A detectable component	The magnitude of the slope of the electrode function $(x\pm\Delta x)$, mV	The percentage of the slope of the function of the electrode $(x\pm\Delta x)$,%
1.	$Pyr_3 [R(W_3O_{10})_4]2H_2O$	Pyridoxine	51.8±0.2	87.9±0.5
2.	$Dim_3 [R(W_3O_{10})_4]2H_2O$	Dibazol	56.2±0.1	96.9±0.4

From the table, we see that the highest value of the slope of the electrode function, equal to 96.9%, corresponds to $Dim_3[R(W_3O_{10})_4]2H_2O$, and the lowest value of this function equal to 87.9% corresponds to $Pir_3[R(W_3O_{10})_4]2H_2O$.

The lower limit of ion selective electrodes in drug detection is one of the main parameters of the electrodeThe linear parts of the E — pA relationship are extrapolated to determine the ion detection limit ($C_{min, p}$) that determines the potential. In this case, the intersection point from which the detection limit of the ion is obtained corresponds to the value of $-lgC_{min, p}$ on the abscissa axis. It was found that the detection limit of pyridoxine selective electrode (pyr-DDFMK) and dibazole selective electrode (Dib-FMK) corresponds to the range of $10^{-5}-10^{-6}$ mol/l.

Figure 3 below shows the results of finding the lowest concentration values of the detectable ion in the determination of dibase using the developed ISE

Figure 3. *Dib3[R(Mo3O10)4]2N2O lower limit of detection of dibazole using ISE with composition*
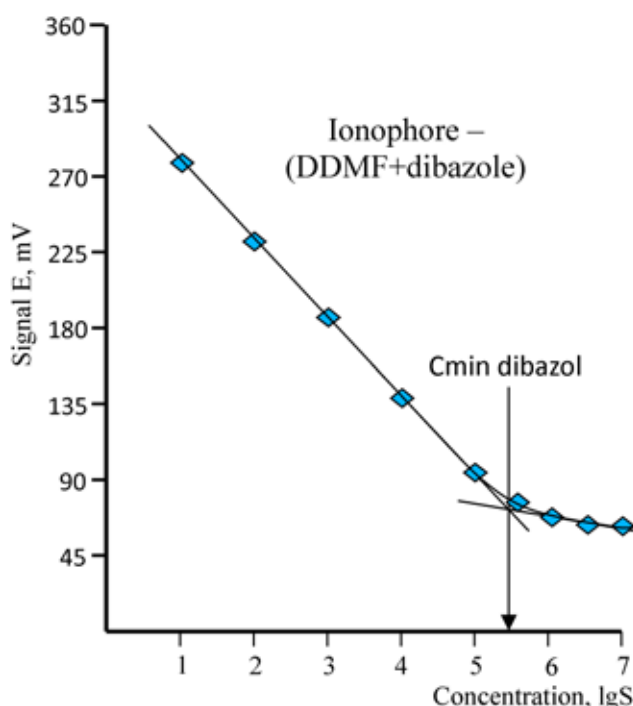
Conclusions

As a result of the research for the express analysis of ori products, ion-selective electrodes with plasticized membranes based on dodecomolybdophosphate heteropolyacid were developed and the effects of various factors on their indicators were investigated.

The optimal conditions for the synthesis of poorly soluble electrode-active compounds (EACs) of medicinal substances with DDMF anion were selected and the electroanalytical properties of the obtained EACs were evaluated.

Methods for obtaining plasticized membranes based on synthesized ionophores have been developed. Effect of EAC physico-chemical properties, membrane and solution composition on potentiometric characteristics of ISEstudied.

The main electrochemical parameters of the developed ISE: the linear range of the signal (of the electrode function), the slope of the electrode function, the lowest limit of ion detection, etc.determined.

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