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Perfluorinated membranes in pd-sensors for determination of components in dosage forms

Bobreshova O.V., Parshina A.V.

The Voronezh State University, Voronezh

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Abstract

The influence of perfluorinated sulfonated cation-exchange polymeric membranes type on the value of PD-sensors sensitivity (the response of PD-sensor is Donnan potential at the PSP membrane/test solution interface) in aqueous solutions of nicotinic acid, pyridoxine hydrochloride, novocaine hydrochloride, lidocaine hydrochloride was studied. The cross-sensitive PD-sensor with pH-selective electrode and reference electrode was used for quantitative determination of vitamins and pharmaceuticals in dosage forms. The multivariate calibration methods with nonorthogonal experimental design were used for calibration of PD-sensors in polyionic solutions. The calibration equations take into account the interference of organic electrolyte concentration and pH of solution on the value of cross-sensitive PD-sensor. The relative error of determination of substances in dosage forms was less than 8%.

Keywords*:* potentiometric sensor; Donnan potential; perfluorinated membranes; vitamins; pharmaceuticals.

Исследовано влияние ионной формы перфторированных сульфокатионообменных мембран на чувствительность ПД-сенсоров (сенсоров, аналитическим сигналом которых является потенциал Доннана на границе мембрана / исследуемый раствор) в растворах никотиновой кислоты и гидрохлоридов пиридоксина, новокаина, лидокаина. Перекрестно чувствительные ПД-сенсоры вместе со стеклянным электродом для измерения pH и хлоридсеребряным электродом сравнения использованы для определения витаминов и лекарственных веществ в фармацевтических формах. Для многомерной градуировки ПД-сенсоров в полиионных растворах использовали неортогональные схемы эксперимента. Калибровочные уравнения учитывали влияние на величину отклика ПД-сенсоров как концентрации органических электролитов, так и pH растворов. Относительная ошибка определения компонентов в фармацевтических формах не превышала 8%.

Ключевые слова: потенциометрические сенсоры, потенциал Доннана, перфторированные мембраны, витамины, лекарственные вещества

Introduction

The perspective tendency in research-and-development work on potentiometric sensors is complex approach, which consists of the using an array of low selective sensors (cross-sensitive sensors) with application of chemometrics for simultaneous quantitative prediction of analytes or qualitative resolution of complex overlapping responses of sensors array [1-8]. Such approach allows to compensate low

selectivity of ion-selective electrodes (ISEs) and to lower detection limit for determination of ionic concentrations in multicomponent aqueous solutions [4-8].

Recently, we described [9, 10] the development of a new type of sensors (PD-sensors), whose analytical signal is the Donnan potential at the ion-exchange membrane/ test solution interface, as cross-sensitive sensors in multicomponent aqueous solutions, containing organic and inorganic electrolytes. The use of the membrane potential equilibrium constant as an analytical signal, which is the Donnan potential at the membrane / test solution interface, allows us to eliminate issues related to migration and diffusion in ionophore-based potentiometric sensors. This process ultimately increases the accuracy, stability and sensitivity of organic and inorganic ion measurements.

Homogeneous perfluorinated sulfonated cation-exchange polymeric (PSP) membranes and tubes, which are Russian analogues of Nafion, were used as an active material in PD-sensors. The structure of PSP membranes is formed by a system of nanopipes (≈1,0 nm) and nanopores (≈5,0 nm) with hydrophobic walls (i.e., polytetrafluoroethylene chains) and hydrophilic sulphonate ionic groups within the channel volumes [11]. PSP membranes are characterized by optimal selective properties as a result of fewer numbers of mesopores and the complete absence of macropores. As a consequence, hydrophobicity of the PSP membranes matrix and complete absence of macropores together provides the increasing of analytical signal, sensitivity and accuracy of PD-sensors in comparison with hydrocarbonic membranes [9, 10]. Thus, the presence of hydrophobic and hydrophilic regions in such membranes provides the matrix with labile structural components, which allows for the electrochemical properties of PSP membranes to be controlled by changing their ionic form.

The protolytic and ion-exchange reactions at the interfaces of membranes and test solutions are potential determinating for the PD-sensors. Thus, the account of influence of the hydronium ions on the sensitivity and stability of the response of PD-sensors in multiionic solutions of vitamins and pharmaceuticals is important.

So, the aim of this paper was to devote the substantiation and practical use of the cross-sensitive PD-sensors for the quantitative determination of vitamins and pharmaceuticals in multiionic aqueous solutions and dosage forms with concentration-correlated ionic forms of organic electrolyte and hydronium ions.

Experimental

Reagents and Apparatus. All chemicals were of analytical reagent grade. All solutions were prepared using distilled water with a resistance of 0.35 MOm·cm. The following analytes of interest were dissolved in aqueous solutions: nicotinic acid (Niacin), pyridoxine hydrochloride (PyridoxinHCl), novocaine hydrochloride (NovHCl), lidocaine hydrochloride (LidHCl). Concentrations of test solutions ranged from $1.0 \cdot 10^{-4}$ to $1.0 \cdot 10^{-1}$ M. The pH values of Niacin, PyridoxinHCl, NovHCl, LidHCl solutions were (3.46-4.65)±0.04, (3.06-4.37)±0.09, (3.87-4.94)±0.03, (5.18-5.82)±0.03, respectively.

Niacin and PyridoxinHCl were determined in dosage forms as tablets and ampoules with concentrations of vitamins 0.05 and 0.01 g, 0.01 and 0.05 g respectively. The amylum and glucose were the adjuvant in tablets. For quantitative determination of vitamins the solutions of dosage forms were prepared. The tablets and ampoules of Niacin were dissolved in 50 ml and 10 ml of distilled water,

respectively. The tablets and ampoules of PyridoxinHCl were dissolved in 25 ml and 10 ml of distilled water respectively. NovHCl and LidHCl were determined in injection solutions containing 0.5 and 2%; 0.5 and 10% of pharmaceuticals, respectively. The injection solutions of NovHCl, LidHCl were not diluted with water.

The PSP membranes as tubes (length is 6 cm, diameter is 0.1 cm, area is 0.02 cm^2, fig. 1) in K^+-type and H^+-type were used as electrodoactive material of PD-sensors.

All solutions were analyzed at 25±0.05^{0}C using a liquid thermostat TJ-TS-01/12. All potentiometric measurements were performed using an Expert-001-3(0.1) fluid analyzer. A glass pH-SE (ELS-43-07) and silver chloride/silver reference electrode (EVS-1M3.1) were used. The reported relative errors for this device for pH and electromotive force (EMF) measurements were 2.5% and 1.5%, respectively.

The method of acid-base titration was used for independent determination of vitamins and pharmaceuticals [12].

Organization principles of PD-sensors. A scheme of an electrochemical cell for quantitative determination of vitamins and pharmaceuticals in aqueous solutions and dosage forms is presented in fig. 1.

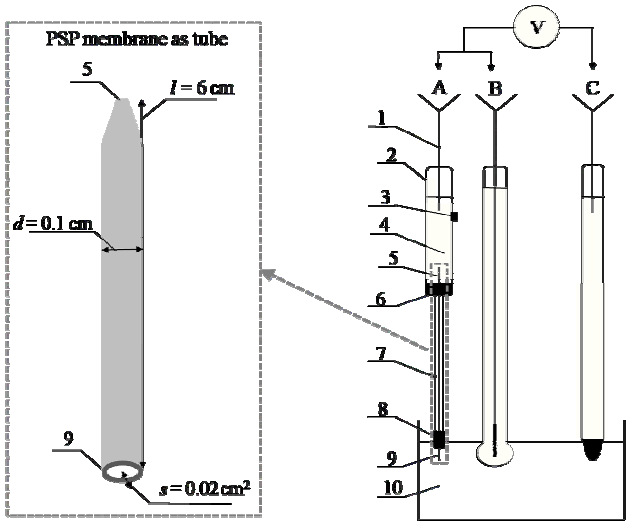

Fig. 1. The scheme of the electrochemical cell for quantitative determination of vitamins and pharmaceuticals in aqueous solutions and dosage forms:
l, d, s are length, diameter, section of tube of PSP membrane; A is the PD-sensor; B is pH-SE; C is silver chloride/silver electrode; V is high resistance voltmeter; 1 is internal reference electrode Ag/AgCl; 2, 7 are plastic encasements with volumes of 5 and 0,5 cm^3, respectively; 3, 6, 8 are rubber stoppers; 4 is internal reference solution; 5, 9 are tips of PSP membrane, which are in contact with internal reference solution and test solution respectively; 10 is the test solution

The sensor array included PD-sensor, pH-SE and a silver chloride/silver reference electrode. The potentials of PD-sensor and pH-SE were measured by the reference electrode using a high resistance electronic voltmeter. The responses from the PD-sensor were registered after 5-7 min, which was the time it took to reach a quasi-equilibrium state [9, 10].

The PD-sensor [9, 10] included two plastic encasements (fig. 1). There was Ag/AgCl electrode in upper encasement (volume is 5 cm^3). There was PSP membrane (as tube) in lower encasement (volume is 0.5 cm^3). The tip of PSP

membrane was in upper encasement. Another tip of PSP membrane projected from upper encasement and was immersed in the test solution. The upper encasement was filled by the reference solution. Depending on the ionic type of the membranes (K^+- or H^+-type)., 1 M solutions of HCl or KCl were used as reference solutions. The lower encasement in work was empty and prevented the PSP membrane from drying.

The electrochemical circuit (eq. (1)) for the determination of the response of the PD-sensor was constructed in the following configuration [9, 10, 13, 14]:

$$\text{Ag}\,|\,\text{AgCl, 1M Cl}^-\,|\,\text{PSP}\,|\,\text{test solution}\,|\,\text{sat. KCl, AgCl}\,|\,\text{Ag}, \quad (1)$$

$$E = \Delta\varphi^{0(\text{A})}_{\text{Ag/AgCl}} + \Delta\varphi^{1\text{M Cl}^-}_{\text{PSP}} + \Delta\varphi_{diff} + \Delta\varphi^{\text{PSP}}_{\text{test solution}} + \Delta\varphi^{\text{test solution}}_{\text{sat.KCl}} - \Delta\varphi^{0(\text{C})}_{\text{Ag/AgCl}}. \quad (2)$$

where $\Delta\varphi^{0(\text{A})}_{\text{Ag/AgCl}}$ and $\Delta\varphi^{0(\text{C})}_{\text{Ag/AgCl}}$ are the standard potentials of an intrinsic reference electrode of the PD-sensor (A) and reference electrode (C) respectively; $\Delta\varphi^{1\text{M Cl}^-}_{\text{PSP}}$ is the potential difference at the interface between the intrinsic reference solution of the PD-sensor (A) and PSP; $\Delta\varphi_{diff}$ is the diffusion potential in the PSP phase; $\Delta\varphi^{\text{PSP}}_{\text{test solution}}$ is the Donnan potential at the interface PSP/test solution; and $\Delta\varphi^{\text{test solution}}_{\text{sat.KCl}}$ is the potential difference at the test solution/KCl saturated solution interface of the reference electrode (C).

A special feature of the organization of such PD-sensors is that the distance between the boundaries of the PSP membrane with the test solution and the reference solution corresponds to the length of the membrane, unlike the case of the known ISEs, in which it corresponds to the membrane thickness. Therefore, in the PD-sensor, the diffusion time of 1 mol of an electrolyte through the PSP membrane (length is 6 cm, area is $(1.6\text{-}5)\cdot10^{-2}$ cm^2, fig. 1) is $5.6\cdot10^6$ hours [9], which is longer than the measurement time (5-7 min) by several orders of magnitude. The diffusion time was calculated for the test solution with a minimum concentration of electrolyte ($1.0\cdot10^{-4}$ M) and the reference solution with a concentration of electrolyte 1 M. It was assumed that the average integral permeability coefficient of the polymer is $\sim10^{-7}$ cm^2/s [11]. During the measurement the quasi-equilibria are formed at the reference solution/membrane and membrane/test solution interfaces, which are stable as a function of time and are independent from each other. Therefore, the diffusion potential in the membrane phase ($\Delta\varphi_{\text{diff}}$) consists of diffusion potential in the volume of phase and diffusion potentials at the membrane interfaces with solutions. In that system the ionic properties and concentrations in the solution phase and the membrane were slightly changed. Therefore, the diffusion potential in the volume of membrane phase is close to zero. The selectivity of the MF-4SC membrane (exchange capacity of 0.8-1.0 mM/g) in solutions with concentrations of no more than $1.0\cdot10^{-1}$ M approaches to ideal. Thus, at the MF-4SC membrane/ test solution interface the Donnan potential difference limits the equalization of the counter-ions and co-ions concentrations in the solution and membrane phases. Therefore, the diffusion potential at the membrane/ test solution interface is close to zero. At the membrane/ reference solution interface, the diffusion potentials decreased even to ~1.1 mV [15] off because of close concentrations of counter-ions and co-ions in connected nano- and mesopores near the phase boundary and in the bulk of the membrane. For these purpose, between analytical measurements, the PD-sensors based on MF-4SC in K-type and H-type should be kept in 0.1 M KCl and 1.0 M HCl solutions,

correspondingly. The diffusion potential at the membrane/ reference solution interface was calculated by the Henderson equation [15]. Thus, we can neglect the value of diffusion potential in the membrane phase ($\Delta\varphi_{diff}$). In electrochemical chains (1) and (2), reference electrodes with equal standard potentials ($\Delta\varphi^{0(A)}_{Ag/AgCl}$ and $\Delta\varphi^{0(C)}_{Ag/AgCl}$) were used, which counterbalance each other. The liquid junction potential ($\Delta\varphi^{test\ solution}_{sat.KCl}$) at the interface between the test solution and the external reference electrode was calculated by the Henderson equation [15]. The $\Delta\varphi^{test\ solution}_{sat.KCl}$ for HCl, NaCl, KCl and $CaCl_2$ solutions with a minimal test concentration ($1.0\cdot10^{-4}$ M) were -4.6, -5.1, -5.1, and -4.8 mV, respectively. The potential difference at the interface between the reference solution of the PD-sensor and the PSP membrane ($\Delta\varphi^{1M\ Cl^-}_{PSP}$) is minimized by the similarity of the concentrations of the reference solution and fixed groups of the PSP membrane. It was calculated that the value of $\Delta\varphi^{1M\ Cl^-}_{PSP}$ at the interface between 1 M solution of a 1:1 electrolyte and PSP membrane with an exchange capacity of 1 mM/g is equal to 2-10 mV [9]. This value was assessed by taking into account the fraction of undissociated fixed groups and groups located in the pores of the PSP membrane, which contain an electrically neutral electrolyte solution. The net contribution of the potential jumps at all phase boundaries of the electrochemical chains (1) and (2), except for the Donnan potential jump ($\Delta\varphi^{PSP}_{test\ solution}$) at the PSP membrane/ test solution interface was -3-5 mV [9]. In this case, the experimental values of the EMF of the chain for the test systems vary in the range of 20-200 mV. Thus, the Donnan potential at the PSP membrane/ test solution interface ($\Delta\varphi^{PSP}_{test\ solution}$) is the analytical signal of a PD-sensor.

Experimental design. Multivariate calibration methods. The stability, sensitivity and selectivity of sensors were estimated in individual solutions of analytes. The determination of activity coefficients in the polyionic systems is a difficult scientific problem. Therefore, calibration of the PD-sensors was performed in the $\Delta ц_D$/pC co-ordinates. In this case, the calibration coefficients include information about the relationship between activity and ion concentration in the phase of a solution and in the phase of the PSP membranes.

The multivariate regression methods were used for calibration of PD-sensors in multiionic solutions. The coefficients of multivariate calibration equations were determined by the method of least squares with nonorthogonal experimental design. The calibration coefficients were compared with determination errors for checking the significance. The spread of the calculated and experimental values of sensor responses was compared with the spread of the results of duplicated experiments for checking the adequacy of calibration equations [16].

Results and discussion

The influence of ionic type of PSP membranes and ion-molecular composition of vitamins and pharmaceuticals solutions on the sensitivity of PD-sensors response. The investigated vitamins and pharmaceuticals are organic ampholyte because various functional groups (-NH_2, =NH, -COOH, -OH) are present in their structure. Therefore solutions of investigated vitamins and pharmaceuticals contain several

organic ionic forms of electrolyte and aqueous dissociation products (H_3O^+ or OH^-) simultaneously. Ionic composition of the investigated solutions was calculated from experimental pH values considering electro neutrality equations, material balance and dissociation constants of organic electrolyte functional groups. It was obtained that in investigated solutions nicotinic acid is presented by both cations ($C_{NiacinH^+}$=0.6·10^{-4}-0.8·10^{-1} M) and zwitterions ($C_{NiacinH^\pm}$=0.4·10^{-4}-0.3·10^{-2} M); pyridoxine hydrochloride, novocaine hydrochloride, lidocaine hydrochloride are presented mainly by the singly charged cations ($C_{PyridoxinH^+}$=0.5·10^{-4}-0.9·10^{-1} M, C_{NovH^+}=1.0·10^{-4}-7·10^{-2} M, C_{LidH^+}=1.0·10^{-4}-3.7·10^{-1} M, respectively). The organic ionic forms of electrolyte and inorganic ions are capable of participating in ion-exchange and protolytic reactions both in the solution and PSP membranes phases, as well as at the membrane/solution interface. Value of the PD-sensor response and distribution of PD-sensor sensitivity depends on the nature and concentration of all ions, which participate in the reactions at the PSP membrane/ test multiionic solution interface.

Fig. 2 represents slopes of calibration function of the from the electrolyte concentration in individual solutions of investigated vitamins and pharmaceuticals. The slope values are characteristics of PD-sensors sensitivity.

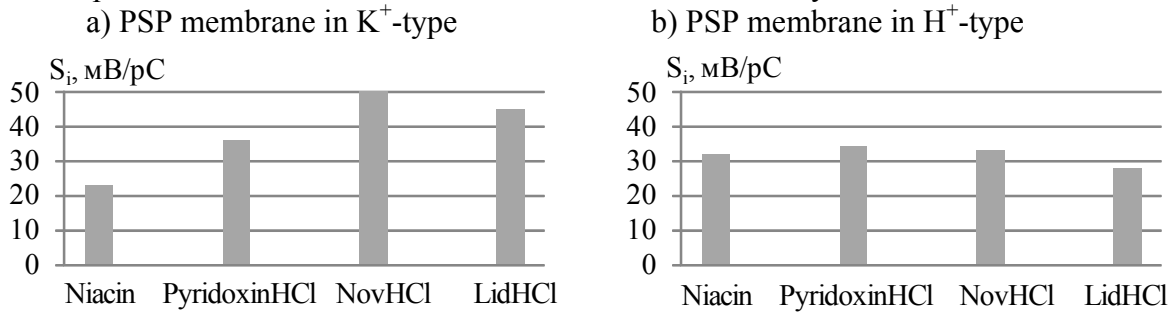

Fig. 2. Sensitivity of PSP-based K^+-type (a) and H^+-type (b) PD-sensors in test solutions of Niacin, PyridoxinHCl, NovHCl, LidHCl

The use of PSP membranes in various ionic forms leads to different PD-sensor sensitivities in solution of the same organic component. The potential determinating reactions of PSP-based K^+-type PD-sensors are ion-exchange reactions (eq. 3). High sensitivity of PD-sensor in solutions of strong organic electrolytes (36±2 mV/pPyridoxinHCl, 51±4 mV/pNovHCl and 45±5 mV/pLidHCl) is caused by the ion-exchange reactions. In case of NovHCl and LidHCl solutions the sorption of large $NovH^+$ and $LidH^+$ ions is complicated by the steric factor.

$$XH^+ + \overline{K^+} \Leftrightarrow \overline{XH^+} + K^+, \qquad (3)$$

where XH^+, K^+ are $NovH^+$ ($LidH^+$), K^+ ions in the solution phases; $\overline{XH^+}, \overline{K^+}$ are $NovH^+$ ($LidH^+$), K^+ ions in the membrane phases.

In comparison with strong electrolytes the sensitivity of PD-sensor in solutions of Niacin, which is a weak electrolyte, is lower (23±2 mV/pNiacin) (fig. 2).

In PSP-based H^+-type PD-sensors, H_3O^+ ions make an additional contribution to the formation of the response. The H_3O^+ ions competed with large organic cations during formation of the Donnan potential at the PSP membrane/ test solution interface. Additionally, the singly charged organic cations $NovH^+$, $LidH^+$ did not participate in ion-exchange reactions. These cations transformed into doubly-

charged ions in the polymer phase as a result of a heterogeneous protolytic reaction (eq. 4). Thus, adsorption at the interface of large doubly-charged ions resulted in the decreased contribution of an organic component to the response.

$$XH^+ + \overline{H_3O^+} \Leftrightarrow \overline{XH_2^{2+}} + H_2O. \quad (4)$$

As a result, the stability of the analytical signal of the PD-sensor in such systems decreased. In some cases, the sensitivity to an organic component also decreased (e.g., by 1.5 and 1.6 times to $NovH^+$ and $LidH^+$, respectively). The sensitivity of the PSP-based H^+-type PD-sensors in solutions of nicotinic acid increased by 1.5 times compared to PSP-based K^+-type PD-sensors (fig. 2). In the PSP-based H^+-type PD-sensors, both cations ($NiacinH^+$) and zwitterions ($Niacin^{\pm}$) of nicotinic acid contributed to the response (eq. 5, 6). The protolytic reactions were the cause of $Niacin^{\pm}$ ion contribution, which resulted in the transfer of cations to the PSP phase.

$$NiacinH^+ + \overline{H_3O^+} \Leftrightarrow \overline{NiacinH^+} + H_3O^+, \quad (5)$$

$$Niacin^{\pm} + \overline{H_3O^+} \Leftrightarrow \overline{NiacinH^+} + H_2O. \quad (6)$$

Thus, PSP-based H^+-type PD-sensor was chosen for determination of Niacin in aqueous solutions. On the other hand, determination of PyridoxinHCl, NovHCl, LidHCl in aqueous solutions was carried out applying PSP-based K^+-type PD-sensor.

In aqueous solutions of vitamins and pharmaceuticals the concentrations of the organic ionic forms of electrolyte and aqueous dissociation products are correlated. The concentration of organic ionic forms of vitamins and pharmaceuticals an order higher than concentration of H_3O^+ ions in test solution. However, as referred in [10], the sensitivity of PD-sensor to H_3O^+ ions is high. Therefore, the calibration model taking into account the interference of several factors was obtained by multivariate calibration methods and is expressed by the eq. (3). These factors are the negative decimal logarithm of total concentrations of X^+ and $X^{\pm}$ (pC) and the pH:

$$\Delta\varphi_D = b_0 + b_1 \cdot pC + b_2 \cdot pH, \quad (7)$$

where $\Delta\varphi_D$ is response of PD-sensor (mV); C is analytical concentration of organic electrolyte (M); b_0 is free term of calibration equations (mV); b_i is sensitivity to coefficients determine the corresponding ion (mV/pC). The coefficients of calibration equations (7) were calculated by using the nonorthogonal experimental design. So they can not be impartial assessment of sensor sensitivity to individual components of solution because they take into account influence of both the ionic forms of organic electrolytes and the H_3O^+ ions on the PD-sensor response.

Table 1 summarizes the coefficients of the calibration equations (3) of PD-sensors in aqueous solutions of Niacin, PyridoxinHCl, NovHCl, LidHCl in the concentration range from $1.0 \cdot 10^{-4}$ to $1.0 \cdot 10^{-1}$ M. The matrix of PD-sensors responses values in investigated solutions contained 7 average values obtained by replicating the experiment 8 times in the same conditions. The calibration equations were found to be adequate at a confidence level of 0.05.

In the Table 1 shows that influence of H_3O^+ ions to PD-sensor response is sufficient. The highest sensitivity of PD-sensors to H_3O^+ ions in Niacin solutions was obtained. Calibration equations, for which coefficients are represented in Table 1, may be used for quantitative determination of Niacin, PyridoxinHCl, NovHCl, LidHCl in solutions and dosage forms.

Table. 1. The coefficients of the multivariate calibration equations (3)

Test solution	Niacin	PyridoxinHCl	NovHCl	LidHCl
Ionic type of PSP membrane	H^+-type	K^+-type		
$b_0 \pm \Delta b_{0\ (p=0.95;f=42)}$, mV	–	–47±3	–23±2	–5±2
$b_1 \pm \Delta b_{1\ (p=0.95;f=42)}$, mV/pC	–20.6±0.5	–40.3±0.4	–62±3	–49±3
$b_2 \pm \Delta b_{2\ (p=0.95;f=42)}$, mV/pH	–30.2±0.2	11.6±0.2	19±3	3±1

Determination of vitamins and pharmaceuticals in dosage forms. The cross-sensitive PD-sensor with pH-selective electrode and reference electrode was used for determination of vitamins and pharmaceuticals in dosage forms as tablets, ampoules and injection solutions. The amylum and glucose, which were the adjuvant in tablets of Niacin and PyridoxinHCl, are nonelectrolytes. Therefore, the ionic forms of vitamins and H_3O^+ ions make the main contribution to response of the cross-sensitive PD-sensors in aqueous solutions of dosage forms. Concentrations of vitamins and pharmaceuticals in solutions of dosage forms were calculated using the calibration equation (7) and the coefficients given in table 1.

The results of determination of vitamins and pharmaceuticals in dosage forms by using the standard titration analysis and potentiometric multisensory system are presented in table 2. The number of replicate measurements was 5. The statistical data interpretation was made using a confidence coefficient of 0.95.

Table 2. Determination of vitamins and pharmaceuticals in dosage forms

Determinate component	Concentration of component in dosage forms, M	pH	Potentiometric multisensory system			Titration		
			C, M	s_r	ΔC/C,%	C, M	s_r	ΔC/C,%
Niacin	$8\cdot10^{-3}$	2.89±0.04	$8.3\cdot10^{-3}$	0.02	4	$8.3\cdot10^{-3}$	0.04	4
	$8\cdot10^{-3}$	4.94±0.04	$8.0\cdot10^{-3}$	0.02	1.8	$7.2\cdot10^{-3}$	0.04	10
PyridoxinHCl	$2\cdot10^{-3}$	3.35±0.05	$1.9\cdot10^{-3}$	0.012	6	$1.6\cdot10^{-3}$	0.2	20
	$2.4\cdot10^{-2}$	2.45±0.05	$2.2\cdot10^{-2}$	0.02	8	$2.5\cdot10^{-2}$	0.02	6
NovHCl	$1.8\cdot10^{-2}$	4.00±0.03	$1.7\cdot10^{-2}$	0.03	6	$1.2\cdot10^{-2}$	0.04	33
	$7.3\cdot10^{-2}$	3.87±0.03	$7.5\cdot10^{-2}$	0.01	3	$7.0\cdot10^{-2}$	0.04	4
LidHCl	$1.8\cdot10^{-2}$	5.74±0.03	$1.7\cdot10^{-2}$	0.03	6	$1.5\cdot10^{-2}$	0.04	17
	$3.7\cdot10^{-2}$	5.81±0.03	$3.6\cdot10^{-1}$	0.01	3	$3.5\cdot10^{-1}$	0.04	5

The comparison of stated composition of dosage forms and determined concentration was used for calculation of relative error of measurement (table 2). It was found that the relative errors of determination of substances by means of potentiometric sensors were 1.8-8 % and did not depend on concentration of vitamins and pharmaceuticals in test solutions. The use of titration for the substances determination gave relative errors within the range 4-33 %. Such results are caused by the low sensitivity of the titrimetric technique in the range of low concentrations. Furthermore, it is advantageous to apply potentiometric sensors for determination of vitamins and pharmaceuticals in dosage forms owing to the possibility of rapid analysis and automation of measurements in contrast to standard titration analysis.

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Bobreshova Olga V. – Doctor of Chemistry, Professor, Department of Analytic chemical, Voronezh state university, Voronezh

Parshina Anna V. – Candidate of. Chemistry, s.em. of analytical chemistry department of chemical faculty, Voronezh state university, Voronezh