

*Розроблено потенціометричні сенсори для визначення концентрації буритинової та салицилової кислот. У якості електродно-активних речовин пластифікованих плівкових мембран використано іонні асоціати цих кислот із сафраніном Т. Встановлено електродно-аналітичні характеристики сконструйованих сенсорів та визначено коефіцієнти селективності по відношенню до карбонових кислот. Проведено потенціометричне визначення концентрації за допомогою розроблених сенсорів у зразках квасу, червоного вина, листі волоського горіха, салицилово-резорциновому розчині та салициловій мазі*

*Ключові слова: потенціометрія, сенсор, буритинова кислота, салицилова кислота, харчові продукти, фармацевтичні препарати*

*Разработаны потенциометрические сенсоры для определения концентрации янтарной и салициловой кислот. В качестве электродно-активных веществ пластифицированных плёночных мембран использованы ионные ассоциаты этих кислот с сафранином Т. Установлены электродно-аналитические характеристики сконструированных сенсоров и определены коэффициенты селективности по отношению к карбоновым кислотам. Проведено потенциометрическое определение концентрации с помощью разработанных сенсоров в образцах кваса, красного вина, листьях грецкого ореха, салицилово-резорциновом растворе и салициловой мази*

*Ключевые слова: потенциометрия, сенсор, янтарная кислота, салициловая кислота, пищевые продукты, фармацевтические препараты*

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# DEVELOPMENT OF POTENTIOMETRIC SENSORS FOR DETERMINING THE CONCENTRATION OF ETHAN-1,2-DICARBOXYLIC AND 2-HYDROXY-BENZOIC ACIDS

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## 1. Introduction

An important contemporary task is to analyse and control the quality of foodstuffs, agricultural raw materials, and pharmaceuticals. To assess the safety of products of food and pharmaceutical industries, it is necessary to control contaminants, food additives (preservatives, sweeteners, antioxidants, dyes, etc.), identify fraud, and assess the quality of manufactured products [1–4]. These issues are traditionally addressed with analytical methods, including gas and high pressure liquid, ion exchange, thin-layer and size-exclusion chromatography, atomic absorption spectroscopy, inductively coupled plasma mass spectrometry, capillary electrophoresis, stripping voltammetry, conductometry, and ionometry.

Determination of the contents of succinic and salicylic acids in the environment, foodstuffs and pharmaceuticals is an expedient task of analytic practice.

Ethane-1,2-dicarboxylic acid (succinic acid, SUA) plays an important role in the human body. It can get to the body with food [5], being contained in tomatoes, apples, wine, and juices. Every day the human body synthesizes about 200 mg of SUA [6]. Its deficiency in the body leads to ailments, weakened defence mechanisms of the body, and disruption of its systems. Toxic effects to humans appear starting from 1.5 g/kg of body weight [7].

2-hydroxybenzoic acid (salicylic acid, SA) has weak antiseptic, irritant and keratolytic properties; it is used in medicine for external use in ointments and solutions to treat skin diseases. Thanks to the antibacterial activity, SA is also used for food preservation [8]. SA is toxic in large doses; the LD<sub>50</sub> is 1.75 g/kg. Pregnant women are not recommended to use products that contain it because of increased risk of Reye's syndrome. The overdose symptoms are: headaches, tinnitus, hearing disorders and vision impairment, nausea, vomiting, abdominal pain, diarrhoea, excessive sweating, low blood pressure and bleeding, impaired consciousness, and cramps.

## 2. Literature review and problem statement

Identification of definable substances in complex biological matrices can be reliable through using a combination of a chromatographic distinction of controlled components and a spectral detection or various combinations of hybrid methods.

The concentration of SUA in objects of a complex matrix is determined by the following methods (the object): spectrophotometry (jelly, a substance for rinsing textiles, a preparation for prevention and treatment of metabolic disorders, a composition for general strengthening; immu-

nomotabolic anthelmintics, a dialysis solution, a disinfecting composition, an injectable form, an aqueous fungicidal composition, a solution against intoxication of animals, a combined nootropic agent [9], a rectal dose form [10]); potentiometry (drinking water [11]); potentiometric titration (dry extract from *Cacalia hastata* [12], leaves of *Cacalia hastata*, blueberries, plantain [13], fern, tomatoes, unripe cherry, and apple); capillary electrophoresis (grape wine [14] and kvass [15]); liquid chromatography (fruit wine); high performance liquid chromatography (*Matricaria recutita*); thin layer chromatography (the bark of *Tilia cordata*, walnut leaves, and amber); alkalimetric titration (*Inula* root, fruit and jelly mass, and apple juice).

The concentration of SA is determined by using chromatographic, electrochemical, optical and hybrid methods of analysis, namely: high performance liquid chromatography (coriander seed, violet [16], meadowsweet ordinary [17, 18], erect cinquefoil [19], *Achillea millefolium* [20], spring barley, effervescent tablets [21], and *Lisinoprilum*); gas-liquid chromatography-mass spectroscopy (*Filipendula ulmaria*, *Thymus dimorphus* [22], and *Thymus marschallianus*); paper chromatography (suppositories); spectrophotometry (an alcohol solution of salicylic acid and resorcinol [23], *Cómarum palústre*, *Centaurea scabiósa* [24], *Filipendula ulmaria* [25]); coulometric titration (an alcohol solution [26]); ionometry (aqueous solutions, salicylic ointment [27–30], and an alcohol solution [31]).

The methods of determining the concentration of SUA and SA have certain advantages and disadvantages. The main advantage of high performance liquid chromatography [32–36], chromatography-mass spectroscopy and other hybrid methods [37–39] is high measurement sensitivity. However, their major disadvantage is the need for expensive equipment and the use of highly toxic organic solvents. Spectrophotometry and alkalimetry are cheap and simple to carry out, but they are much less sensitive.

The potentiometric method provides express control of the determinable component without changing the composition of the sample (non-destructive) and in a wide range of content; it is characterized by sufficient selectivity and accuracy; it is convenient, easy and affordable [4, 40–42]. Potentiometer sensors can also operate in a flow analysis mode; they are easy to miniaturize for use as microelectrodes [43, 44]. These benefits have secured potentiometric sensors their rightful place in the process control, routine analysis of industrial and domestic wastes, as well as in the analysis of pharmaceuticals [40, 41], bioliquids [42], foodstuffs [4], cosmetics, and detergents. A large number of studies have been devoted to the use of ion-selective electrodes (ISE) in the pharmaceutical, clinical and biomedical analysis [45–48]. The above ionometric methods [27–30] of determining the content of salicylate ion require specific expensive reagents. Consequently, it is expedient and reasonable to develop a new ionometric method that would be relatively cheap, simple to implement, and sufficiently sensitive.

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### 3. The aim and tasks of the study

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The aim is to develop a sensitive, expressive and simple potentiometric method for determining the concentration of succinic and salicylic acids in foodstuffs and pharmaceutical preparations by using membrane sensors.

The aim is achieved by solving the following tasks:

- to construct sensors based on ion associates of succinic and salicylic acids with safranin T, which are inverse to salicylate ions and succinate ions in solutions;
- to set electrode-analytical and operational characteristics and coefficients of selectivity regarding the proposed sensors as to carboxylic acids and inorganic ions;
- to conduct testing of the developed methods on real objects such as samples of kvass, red wine, walnut leaves, a solution of salicylic acid and resorcinol, and salicylic ointment;
- to compare the results of the suggested potentiometric methods of determining the contents of succinic and salicylic acids by an alternative alkalimetric method.

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## 4. Materials and methods of research applied for developing potentiometric sensors that are sensitive to salicylate ions and succinate ions in solutions

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### 4.1. Reagents and equipment that were used in developing potentiometric sensors for determining the contents of ethane-1,2-dicarboxylic and 2-hydroxybenzoic acids in solutions

We used: safranin T (ST) as a cationic dye, ethane-1,2-dicarboxylic acid (succinic acid, SUA) and 2-hydroxybenzoic acid (salicylic acid, SA), dibutyl phthalate as a plasticizer, cyclohexanone as a membrane solvent, PVC C40 as a matrix, as well as  $H_3BO_3$ ,  $H_3PO_4$ ,  $CH_3COOH$ , and  $NaOH$ . All reagents were chemically pure or chemically pure for analysis. The initial solutions were prepared from accurately weighed substance components, and the solutions of the given concentrations were made by diluting the initial solutions.

According to the ionometric method of determining the concentrations of ethane-1,2-dicarboxylic and 2-hydroxybenzoic acids, the analytical signal was represented by a difference of the galvanic cell potentials, consisting of an indicator electrode and a reference electrode immersed in the test solution. The reference electrode was a silver chloride electrode EVL-1M3 filled with a 0.1 mol/L solution of KCl. The indicator electrodes were manufactured membrane sensors with the contact part EV-Cl-01. The internal solution was ethane-1,2-dicarboxylic and 2-hydroxybenzoic acids of a concentration of  $1 \cdot 10^{-3}$  mol/L. The difference of the galvanic cell potentials was measured by the ionomer EV-74.

The absorption spectra in the visible region were registered by Specord M40.

### 4.2. Establishment of the optimal ratios of EAS components of a sensitive membrane

The electrode active substances were represented by ion associates of ethane-1,2-dicarboxylic and 2-hydroxybenzoic acids with safranin T. An interaction between the cationic dye ST with ethane-1,2-dicarboxylic and 2-hydroxybenzoic acids was established on the basis of the absorption spectra of these agents and their ionic associates. A saturation method according to [49] was used to determine the maximum yield of ion associates of SUA-ST and SA-ST at a certain ratio of the components. This ratio was used as the best option in the preparation of the EAS of sensitive membranes.

### 4.3. Synthesis of PVC membranes (sensitive elements such as ICE)

Plastified PVC sensor membranes, which are sensitive to the concentration of salicylic acid and succinic acid, were synthesized by the standard method [4, 40–42].

The EAS was prepared by draining aqueous solutions of SUA or SA and an organic reagent with adding a universal buffer to obtain a certain value in pH. The EAS synthesis conditions are given in Table 1.

Table 1

The conditions of synthesizing electrode active substances for succinate- and salicylate-selective electrodes

The EAS	$m_{EAS}, g$	The ratio of the dye to the acid	pH
ST-SUA	0.0050	1:1	2.9
ST-SA	0.0050	1:1	6.1

The resulting ionic associates were dried at room temperature and dissolved in the plasticizer at the synthesis of the membrane.

#### 4.4. A method of determining the selectivity coefficients of the designed sensors

The stability, sensitivity and selectivity of the designed sensors as to succinic acid and salicylic acid were assessed through using individual solutions of these acids of concentrations from  $1 \cdot 10^{-2}$  mol/L to  $1 \cdot 10^{-9}$  mol/L and aqueous solutions of carboxylic acids: citrate, tartaric, acetic and oxalic acids as well as inorganic ions:  $K^+$ ,  $Na^+$ ,  $Mg^{2+}$ ,  $Fe^{3+}$ ,  $Br^-$ ,  $I^-$ ,  $Cl^-$ ,  $NO_3^-$ ,  $SO_4^{2-}$ ,  $PO_4^{3-}$ . The selectivity coefficients for the designed sensors were calculated by the method of individual solutions [50].

#### 4.5. The research materials and methods

A sample preparation of walnut leaves to determine SUA is described below. A 2.5 g sample of pre-ground walnut leaves was extracted with a 70 % ethanol until a complete exhaustion of the raw material. The extracts were combined and evaporated to the aqueous residue, which was further cooled and filtered. Then the materials were extracted with equal volumes of chloroform, and the organic solvent was separated. The aqueous residue was heated to remove the chloroform, and after that it was cooled again. Then extraction was performed with ethyl acetate. The aqueous residue was again heated, cooled and treated with 5 mL of isopropyl alcohol.

The study was carried out using direct potentiometry [50], spectrophotometry [49], and alkalimetry [51].

### 5. The research results on the synthesized succinate and salicylate sensors

#### 5.1. Determining the optimum ratio of the components of EAS membranes selective to succinate anions and salicylate anions and the conditions of the sensors' operation

At the pH of 2.5–9.5, the organic reagent ST exists in the cationic form of  $R^+$  with the maximum absorption spectrum at  $\lambda=490$  nm. When the aqueous solution of SUA or SA is added to the ST, the maximum absorption spectrum shifts bathochromically to 10 nm and 11 nm, respectively, and the intensity of the absorption spectrum of the two-component system increases almost twice (Fig. 1, Table 2). This indicates the formation of the associates of ST-SUA and ST-SA (Fig. 1). The method of saturation determined the ratio of the components in the associates under conditions of their

maximum output. The generalized chemical and analytical characteristics of the associates are given in Table 2.

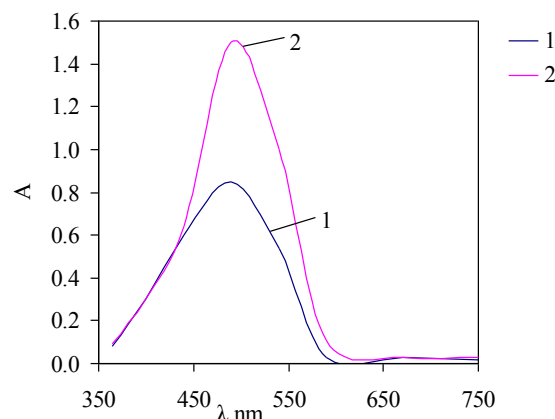


Fig. 1. The absorption spectra of the aqueous solutions – dependence of the absorbance  $A$  on the wavelength  $\lambda$ , nm for the solutions: 1 – ST, 2 – ST-SA,  $S_{ST} = 5 \cdot 10^{-5}$  mol/L;  $S_{SA} = 4 \cdot 10^{-5}$  mol/L; pH of 6.1;  $l = 1$  cm

Table 2

The chemical and analytical characteristics of the studied systems

The system	$\lambda_{max}, nm$	pH <sub>optimal</sub>	$\epsilon \cdot 10^{-4}$	The ratio of the dye to the acid
ST	490	2.8–3.5	1.84	–
ST-SUA	500	2.8–3.8	3.87	1:1
ST	492	5.8–6.3	1.78	–
ST-SA	503	5.6–6.5	3.95	1:1

The possibility to use the cationic dye ST to obtain the EAS is limited by a number of criteria: stability of the dye molecules to various external effects; high solubility of the ion associate with SUA or SA in the membrane solvent, which was dibutyl phthalate; a sufficient ratio of distribution of the ion associate between aqueous and organic media (phase membranes); presence of feedback of the designed plasticized membrane to the analyte ions (SUA or SA).

The ionometry is based on the process of distributing charged particles between the analyte solution sample and the membrane phase solution that provides the appearance of a potential distribution on the verge of the phases. The electrochemically-active compounds SUA-ST and SA-ST, which are located in the sensor membrane, are the determined share as an associative complex with a negative ion.

The response of the polymeric membrane sensors with the EAS on the basis of the ionic associates of ST-SUA and ST-SA was obtained at different concentrations of an internal solution of SUA or SA in the range of  $1 \cdot (10^{-1} - 10^{-5})$  mol/L. It has been found that the best results in terms of the slope of the electrode function and the dynamic range of concentrations were obtained for the internal solution with a concentration of the detectable substance (SUA or SA)  $C = 1 \cdot 10^{-3}$  mol/L.

The resulting electrode functions of the designed sensors for determining the concentrations of SUA and SA were determined without conditioning and after conditioning during 1, 2 and 3 days (Fig. 2, 3). The process of conditioning was used to enhance the synthesized membranes.

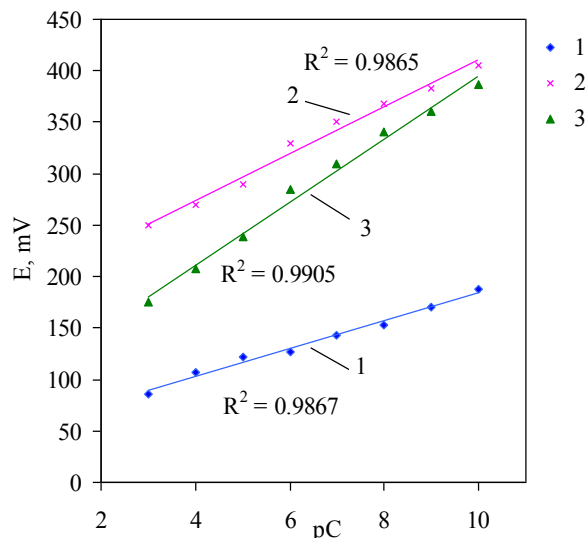


Fig. 2. A dependence of the potentials of E of the membrane sensor with the EAS: ST-SUA on the concentration of SUA pC in the solution at the conditioning of the membrane: 1 – without conditioning; 2 – 1 day; 3 – 2 days ( $R^2$  is the correlation coefficient)

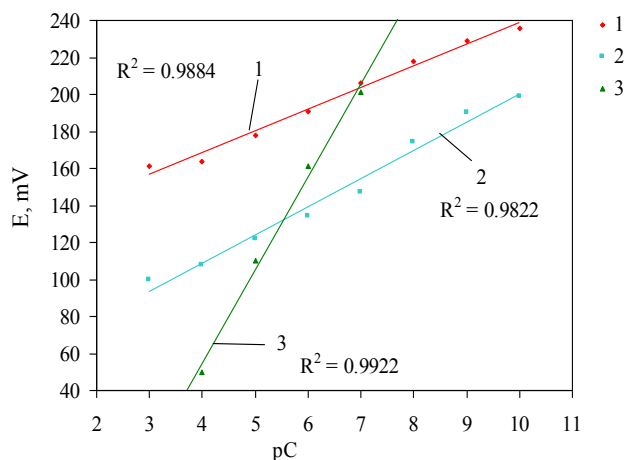


Fig. 3. A dependence of the potentials of E of the membrane sensor with the EAS: ST-SA on the concentration of SA pC in the solution at the conditioning of the membrane: 1 – without conditioning; 2 – 1 day; 3 – 2 days ( $R^2$  is the correlation coefficient)

The sensor of the EAS: ST-SUA has the best analytical electrode characteristics after conditioning for 2 days. The results are reproducible, the electrode function slope of  $S=31 \text{ mV/pC}$  is close to theoretical for a doubly charged anion; the linearity range is of 3 to 10 units of pC (Fig. 2, Curve 3, Table 3). For the sensor on the basis of the ion associate of ST-SA, the optimal time of conditioning of the membrane also was 2 days (Fig. 3, Curve 3, Table 3), with the interval of the linear electrode function of  $10^{-7}$ – $10^{-4} \text{ mol/L}$ , and the slope of  $49 \text{ mV/pC}$ . The summarized data on the effect of the conditioning time on the electrode-analytical characteristics of the of the proposed sensors are shown in Table 3.

To determine the operation interval of the developed sensors that are reversible to SUA or SA, their electrode characteristics were studied in the pH range of 2.0–9.0 of the external solution. The required value of acidity of the external solution

of SUA or SA in the concentration range of  $1 \cdot (10^{-10} - 10^{-3}) \text{ mol/L}$  was determined by adding a certain amount of a universal buffer. The study has revealed that the designed sensors provide reproducible results in a sufficiently wide pH range of 5.5–9.0.

Table 3

The analytical characteristics of the electrodes of the devised sensors with conditioning of the membranes in solutions of the determined substance (SUA or SA),  $C=1 \cdot 10^{-3} \text{ mol/L}$

The EAS	Without conditioning		The conditioning time					
			1 day		2 days		3 days	
	pC	S, mV/pC	pC	S, mV/pC	pC	S, mV/pC	pC	S, mV/pC
ST-SUA	3–10	16	3–10	25	3–8	31	3–10	10*
ST-SA	3–10	12	3–10	15	4–7	49	3–7	10*

Note: \* – irreproducible results

Metrological characteristics of the potentiometric sensors depend on the concentration of the EAS in the membrane phase and the process of its leaching from the membrane in the test solutions. The so-called “self-service” of the sensor systems consists in the fact that at low concentrations ( $10^{-8}$ – $10^{-10} \text{ mol/L}$ ) the sensor responds to the ions of the analyte (SUA or SA) that got into the test solution from the membrane phase. This membrane contains a relevant ion associate. Thus, the detection limit and the sensitivity of the sensor system directly depend on the coefficient of distributing the EAS between the test solution and environment of the membrane. The optimal performance sensors are observed in the suggested sensors in the range of 3–8 points pC.

The drift of the sensors’ potential on the basis of the ion associates of ST-SUA and ST-SA does not exceed 2–3 mV/day; the response time is 1 minute for the solutions at low concentrations of  $1 \cdot (10^{-5} - 10^{-10}) \text{ mol/L}$ . The minimum detectable concentrations are  $C_{\min}=9.5 \cdot 10^{-8} \text{ mol/L}$  (for SUA) and  $C_{\min}=7.5 \cdot 10^{-8} \text{ mol/L}$  (for SA). The optimum time of conditioning is 48 hours. The lifetime of the synthesized membrane does not exceed 10 months. The membrane should be replaced after 40 measurements.

### 5. 2. Determination of selectivity coefficients for succinate and salicylate sensors

Selectivity of film electrodes depends on a difference of free energies of resolution of ions in the transition from the aqueous phase into the membrane. The interfering effects of other organic (citrate, tartaric, acetic acid and oxalate) and inorganic particles is manifested in the reduction of the angular coefficient of the Nernst equation. The selectivity ratios were determined by using membrane sensors with the EAS: ST-SUA and ST-SA. The selectivity of the factors was determined by the method of individual solutions [50]. The results are shown in Table 4, 5.

The data on the selectivity ratios (Table 4, 5) make it possible to assert sufficient selectivity of the developed succinate and salicylate sensors.

The selectivity coefficients for the developed sensors relative to the particles of organic and inorganic nature are in the range of  $1 \cdot 10^{-3}$ – $5 \cdot 10^{-2}$ . Thus, the research results have revealed sufficient selectivity of the devised sensors and the possibility of their use in the analysis of foodstuffs, plant material, and pharmaceuticals.



Table 4

The selectivity coefficients of the membrane sensors with the EAS: ST-SUA

The interfering substance/ion	$K_{sel}$	The interfering substance	$K_{sel}$
$K^+$ , $Br^-$ , $I^-$	$1.0 \cdot 10^{-2}$	glucose; tartaric acid	$5.0 \cdot 10^{-2}$
$Na^+$ ; $Cl^-$	$5.0 \cdot 10^{-2}$	oxalic acid; citrate acid; acetic acid	$1.0 \cdot 10^{-3}$
$Mg^{2+}$ ; $NO_3^-$ ; $SO_4^{2-}$	$3.0 \cdot 10^{-3}$		
$Fe^{3+}$ ; $PO_4^{3-}$	$1.0 \cdot 10^{-3}$	salicylic acid	$3.0 \cdot 10^{-3}$

Table 5

The selectivity coefficients of the membrane sensors with the EAS: ST-SA

The interfering substance/ion	$K_{sel}$	The interfering substance	$K_{sel}$
$K^+$ , $Br^-$ , $I^-$	$2.0 \cdot 10^{-2}$	glucose; tartaric acid	$5.0 \cdot 10^{-2}$
$Na^+$	$3.0 \cdot 10^{-2}$	oxalic acid; citrate acid; acetic acid; succinic acid	$1.0 \cdot 10^{-3}$
$Mg^{2+}$ ; $NO_3^-$ ; $SO_4^{2-}$ ; $Cl^-$	$3.0 \cdot 10^{-3}$		
$Fe^{3+}$ ; $PO_4^{3-}$	$5.0 \cdot 10^{-3}$		

### 5.3. Determination of the SUA content in samples of food and plant material

The content of SUA was determined by the method of additives in samples of kvass, red wine and an extract of walnut leaves through preparing a series of solutions. For this purpose, 5 ml samples of kvass, red wine, and an extract of walnut leaves were placed in 25-ml flasks along with 0, 1, and 2 ml of a standard solution of SUA with a concentration of  $1 \cdot 10^{-5}$  mol/L. The total volume of each solution was 15 ml. The potentials of the resulting solutions were measured by the universal ionometer EV-74.

The results of determining the content of SUA in samples of food and plant materials by direct potentiometry were compared with the results of the alternative alkalimetric method. The alkalimetric determination was performed in the following way: the samples were selected in the amount of 5 ml, placed in 25-ml flasks, and adjusted to the label by double-distilled water. The resulting solution was titrated with a 0.1010 mol/L NaOH solution in the presence of a phenolphthalein indicator. The titration was continued until the pink colour started to disappear within 30 seconds. The determined results are summarized in Table 6.

Since the determined F-criterion is smaller than the tabular value, the differences between the  $S_{potent}$  and  $S_{alcal}$  are insignificant; under ceteris paribus analyses, the data that can be obtained by the potentiometric method are characterized by good reproducibility. The proximity of the average results of determining SUA with the help of the developed sensor by the method of alkalimetry demonstrates correctness of the data obtained by using the developed technique.

Table 6

The results of determining the SUA content in samples of foodstuffs and plant materials ( $P=0.95$ ;  $n=3$ )

The object	Potentiometry		Alkalimetry		Previous research data, mg/L
	The determined C, mg/L	$S_r$ , %	The determined C, mg/L	$S_r$ , %	
Kvass	$1.63 \pm 0.12$	4.4	$1.60 \pm 0.11$	4.3	0.50–15.28
Red wine	$0.11 \pm 0.01$	5.0	$0.11 \pm 0.01$	4.0	0.07–1.75
Walnut leaves	$7.41 \pm 1.08$	5.8	$7.33 \pm 1.11$	5.5	6.44–8.86

### 5.4. Determination of the content of 2-hydroxybenzoic acid in samples of pharmaceuticals

The concentration of 2-hydroxybenzoic acid was determined by using the suggested ionometry method on additives in such objects as a solution of salicylic acid and resorcinol as well as in salicylic ointment. The accuracy of the results was tested by the alternative alkalimetry method.

Table 7

The results of determining the content of 2-hydroxybenzoic acid in pharmaceuticals ( $P=0.95$ ;  $n=3$ )

The object	Potentiometry		Alkalimetry		Declared by the manufacturer, g/L
	The determined C, g/L	$S_r$ , %	The determined C, g/L	$S_r$ , %	
Salicylic ointment	$1.85 \pm 0.21$	4.6	$1.86 \pm 0.17$	4.1	2.0
A solution of salicylic acid and resorcinol	$9.98 \pm 0.93$	4.0	$10.03 \pm 1.43$	4.7	10.0

The results of the potentiometric determination of the concentration are close enough to the content of 2-hydroxybenzoic acid in the pharmaceuticals as claimed by the manufacturer.

## 6. Discussion of the results of developing the potentiometric sensors for determining ethane-1,2-dicarboxylic and 2-hydroxybenzoic acids in foodstuffs and pharmaceuticals

The screening of the EAS on the basis of the ionic associates has showed that the best chemical and analytical properties can be observed in ST-SUA and ST-SA. They are characterized by high solubility in the dibutyl phthalate plasticizer and the ability of being implanted in structural vacancies that are formed by polyvinyl chloride and the plasticizer. This allows their using as an EAS of sensor materials. The obtained potentiometric results are reproducible, and the linear range is wide enough, which is  $1 \cdot (10^{-3} - 10^{-8})$  mol/L. It confirms the possibility of using the developed succinate and salicylate sensors during the analysis of various objects (foodstuffs, plant material, and pharmaceuticals). The suggested sensors comply with the requirements (the response time is 1 minute) that are set for quality control of foodstuffs and pharmaceuticals. The slope of the electrode function of the succinate sensor is 31 mV/pC, which is close to the theoretical value

for double-charged acid residue of SUA. For the salicylate sensor, the electrode function slope is 49 mV/pC, which is a suitable sensitivity for determining singly charged organic anions. For proper functioning of the constructed sensors, it is necessary to pre-condition them in a solution of the determined substance for 2 days. The lifetime of the proposed sensor is 11 months if the sensitive membranes are stored in a desiccator. Reproducibility of the results deteriorates after 40 measurements by one and the same sensor, which entails a need to replace the membrane.

The estimated coefficients of selectivity to inorganic and organic components are within  $1 \cdot 10^{-3}$ – $5 \cdot 10^{-2}$ . This supports the use of the proposed sensors in the 500-fold and 1000-fold surplus of organic and inorganic ions. Determination of SUA and SA is not hindered by the complex matrix of red wine, kvass, walnut leaves, the solution of salicylic acid and resorcinol as well as salicylic ointment. Overall, the selectivity of the developed direct potentiometric methods is higher than of the known ones [27–30].

The developed potentiometric methods that use sensors on the basis of ion associates of SUA and SA with safranin T are sensitive: the minimum detectable concentrations are  $9.5 \cdot 10^{-8}$  mol/L (for SUA) and  $7.5 \cdot 10^{-8}$  mol/L (for SA). The known hybrid methods have a lower detection point only with the use of expensive equipment design, which is not always economically feasible. The suggested succinate and salicylate sensors are sufficiently sensitive, being available.

The experimental data (Table 5, 6) confirm the accuracy of the results of determining the concentration of ethane-1,2-dicarboxylic and 2-hydroxybenzoic acids in samples of foodstuffs, plant material and pharmaceutical preparations by direct potentiometry and absence of a systematic error. The relative standard deviation developed by the potentiometric methods does not exceed 5.8 %.

The results obtained by the potentiometric and alkalimetric methods were evaluated by using the Fisher criterion. As  $F_{\text{exp}} < F_{\text{tabl}}$ , the differences between the  $S_{\text{potent}}$  and the  $S_{\text{alkal}}$  are negligible. The developed potentiometric methods are characterized by good reproducibility. The proximity of the averages of determining the concentration of SUA and SA with the help of the designed sensors and by the alkalimetric method proves the accuracy of the data obtained by using the developed technique.

The suggested technique is sufficiently sensitive and selective, expressive, simple to use, correct, and it yields reproducible results.

The proposed succinate and salicylate potentiometric sensors on the basis of ion associates can be used in pharmaceutical analysis and for quality control of food products, including samples of kvass, red wine, extracts from the walnut leaves, salicylic ointment, and the solution of salicylic acid and resorcinol.

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## 7. Conclusions

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1. The spectrophotometry has helped determine the optimal conditions of synthesizing ionic associates of ethane-1,2-dicarboxylic and 2-hydroxybenzoic acids with safranin T: the ratio of 1:1, pH of 2.9 and 6.1, respectively. We have designed succinate and salicylate sensors in which the sensing element is a PVC membrane that contains implanted ionic associates of salicylic and succinic acids with safranin T.

2. The method of direct potentiometry was used to determine analytical electrode parameters (the slope of the electrode function was 31 and 49 mV/pC, the linear range was 4–7 and 3–8 pC, and the best time conditioning was 24 hours) and performance characteristics (the drift potential was 2.3 mV/day, the response time was 1 min, and the lifetime was 11 months) of the developed sensors. We have determined the selectivity coefficients as  $1 \cdot 10^{-3}$ – $5 \cdot 10^{-2}$  for the produced succinate and salicylate sensors by individual solutions with respect to inorganic and organic components. These values confirm the usability of the sensors to analyse objects with a complex matrix.

3. The suggested potentiometric methods for determining the concentrations of ethane-1,2-dicarboxylic and 2-hydroxy acids were tested on samples of food products (kvass and red wine), plant material (walnuts leaves) and pharmaceuticals (salicylic ointment and the solution of salicylic acid and resorcinol). The correctness of the developed methods and absence of a systematic error were confirmed by the method of additives.

4. Samples of food, plant material and pharmaceuticals were analysed by the alternative alkalimetry method. The comparison of the obtained results by the two methods has proved equal reproducibility of the newly developed and alternative methods. According to the Fisher criterion, the methods do not have any significant difference.

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