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The New Mephenaminate- and Phenylanthranilate-Selective Membrane Sensor

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Abstract- Mefenamic acid (Mef) is a derivative of phenylanthranilic acid (Paa). As a drug of the NSAID group, it reduces the sensation of pain and suppresses the development of inflammation in the human body. For its determination, in substance and dosage forms (tablets, capsules, gels) different methods of analysis are used. Ionic associate (IA) compounds of Mef and Paa with rhodamine 6G were used as electroactive substances (EAS) in the manufacture of membranes of ion-selective electrodes. Investigation of the electrochemical properties of the obtained ISEs with different contents of the EAS (1-10%) shows that they give an answer to the concentration of Mef and Paa in a solution in a wide range: 5×10^{-4}-1×10^{-2} and 2×10^{-3}-1×10^{-1} mol/l, with the slope of 83.1 and 89.1 mV/pC respectively. The content of the EAS in the composition of the membrane with a content of 4-8% slightly affects the basic electroanalytical characteristics of the sensors manufactured. Further, an increase in the content of the associate leads to thickening and increases the rigidity of the membrane, which causes the deterioration of the steepness value and the limits of detection of the test substance. Significant influence on the results of the work of the electrodes may alter the quantitative content of the plasticizer in the membrane. The research was carried out for membranes containing DBF of 35-75%. As a result of measurements, it was found that electrodes with content of plasticizer of 45-70% possess good electroanalytical characteristics. The operating range of the acidity of the functioning of the electrode is equal to the pH range 9-11. Stable values of electrode potentials are set within 5-10 seconds. Synthetic membranes are suitable for work for at least 4 months. Efficient techniques of the potentiometric determination of the content of mefenamic and phenylanthranilic acids in model solutions and pharmaceuticals were developed.

Keywords- Potentiometry; Sensor; Mefenamic acid; Phenylanthranilic acid

1. INTRODUCTION

The problem of the quality control of drug preparations remains actual for modern analytical chemistry. This is caused by the growth of the number of drugs (of different companies) registered in the pharmacopeia, like also the introduction of novel highly active substances, belonging to the novel classes of natural and synthetic compounds. Another factor influencing this question is the economic changes in the market of drugs, caused by the introduction of new substances to the market alongside the ready preparations [1]. Thus, the development of methodologies, permitting a rapid and exact drug determination in preparations without separation or preliminary concentration is necessary.

Mephenaminic acid (Mef) is a phenilanthranilic acid (Paa) derivative. It is a pain-killer and anti-inflammatory drug, suppressing the inflammation process in the human organism. Nevertheless, its advantage, while confirmed with other drugs of the same group is its immunostimulating and fever-killing action, the reason why Mef is frequently used in medical practice [2,3].

The issues of quality control of pharmaceutical products remain relevant to modern analytical chemistry. This is due to an increase in the number of registered pharmacopeia medicines (often different manufacturers) and the introduction of pharmaceutical practices of high-level substances belonging to the new classes of natural and synthetic compounds, and economic changes in the pharmaceutical market through the introduction of the scope of treatment at the international and regional levels of various substances in addition to ready-made drugs.

Many analytical methods are used to detect this substance in pharmaceutical preparations (pills, capsules and gels), including chromatographical [4–10], spectophotometrical [11–20], potentiometrical, including potentiometrical titration [21,22], voltammetrical [23,24] atom absorption spectroscopy [25], NMR spectroscopy [26], non-aqueous and biphase titration [27,28]. Nevertheless, all of the mentioned methods may represent certain disadvantages, due to their complexity in operation, difficulties in analytical signal interpretation, slow response and use of expensive materials and lab equipment, which offers to search for an alternative .
The ionic associate (IA) compounds and their use in the quantitative analysis are intensively investigated. Many works, using IA as electroactive substances (EAS) for ion-selective electrodes (ISE) for the analytical determination of biologically active substances have been published recently [21,29,30]. Nevertheless, only one potentiometric technique for mephenaminic acid employing an ion-selective sensor is known. Yet for phenylanthranilic acid, none are known.

Therefore, the goal of this work is the development of the plastified membrane potentiometric sensors for mephenaminic and phenylanthranilic acids with their ion associates with the Rhodamine 6G (R6G) basic dye (BD), Fig. 1, as EAS.

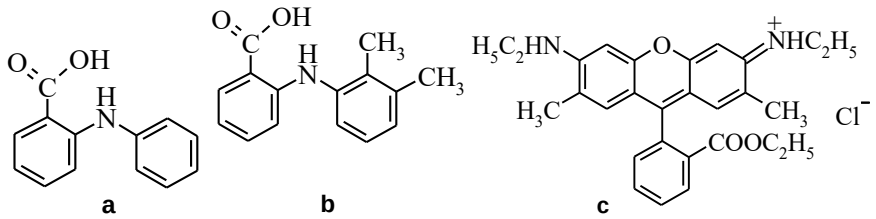

Figure 1. Mephenaminic acid (a), phenylanthranilic acid (b) and Rhodamine 6G (c)

When solutions of dye with mefenamine and phenylanthranilic acid are mixed, there are noticeable changes in the light absorption of systems. With an increase in the Mef or Paa concentration, provided that the Rh6G content is stable, a bathochromic displacement of the absorption band of the dye is observed, which can be attributed to the formation of a compound of the type of ionic associates. The appearance of an isosbestic point at 533 nm indicates the formation of compounds of constant composition, and a decrease in the maximum absorption of OD (25-30%) with insignificant amounts of antioxidants 8×10^{-5} mol/L, confirms the intense association of Rh6G with the acids under study. The formation of ionic associates also indicates the received IR spectra.

2. EXPERIMENTAL SECTION

The initial phenylanthranilic and mephenaminic acid solutions (1×10-^{1} and 1×10^{-2} mol/l) were prepared by dissolving exact mass samples of their crystalline forms in small quantities of 0.2 mol/l NaOH. The pH value was set to 9.0 by a universal buffer. The solution was diluted to the mark by distilled water. The lower concentrations solution series (1×10^{-2} to 1×10^{-6} mol/l) were prepared by the consequent dilution from the initial solutions **.**

The initial Rhodamine 6G 0.02 mol/l solution was prepared by the dissolution of the exact mass sample, recrystallized in methanol, in distilled water**.**

The IA was deposited by stirring 0.2 mol/l Mef or Paa solutions with R6G (1:1). The mixture was stirred and kept at RT for 8 – 10 hours. The IA was filtered out, rinsed several times by distilled water, and dried in the open air at room temperature**.**

The plastified PVC membranes were prepared according to [31]: 0.075 g of PVC and the necessary quantity of the correspondent IA (up to 10 % of the membrane mass) were intensively stirred in a china melting pot. 0.15 ml of plastifier, 0.5 ml of THF were accurately stirred to yield the homogenous mass. The plastifiers were dibutylphthalate (DBP), dioctylphthalate (DOP), dibuthylsebacinate (DBS), dinonylphthalate (DNP) and tricresylphosphate (TCF). The mixture was put into the dry form (glassy ring with the diameter 1.8 cm, fixed to the glassy basement), and kept for 1 – 2 days. A disk of the necessary diameter was cut off the resulting films and fixed to the end of the PVC tube**.**

The potentiometric measures were carried out by ionometers AI–123 and Ecotest-120 with the eight-channel commutator at RT. The chlorine-silver electrode EVL-1M3 has been used as a reference electrode. The pH was maintained by a universal buffer, obtained by mixing of 0.2 mol/l NaOH with acid mixtures of 0.04 mol/l of H_3BO_3, H_3PO4, and CH_3COOH in certain relations. pH of the obtained solutions was controlled potentiometrically by AI–123 ionometer with glass electrode at RT **.**

The absorption spectra of the solutions, containing the BD or its IA were fixed by SF-2000 Spectrophotometer (LOMO, Russia) in the 400 – 800 nm interval.

The IR spectra of the electroactive substances and dye salt were carried out on IR spectrometer Nicolet iS10 with Continuum IR microscope in a reflection-permeability mode in the metalized glassy vessel in 4000–650 cm^{-1} interval.

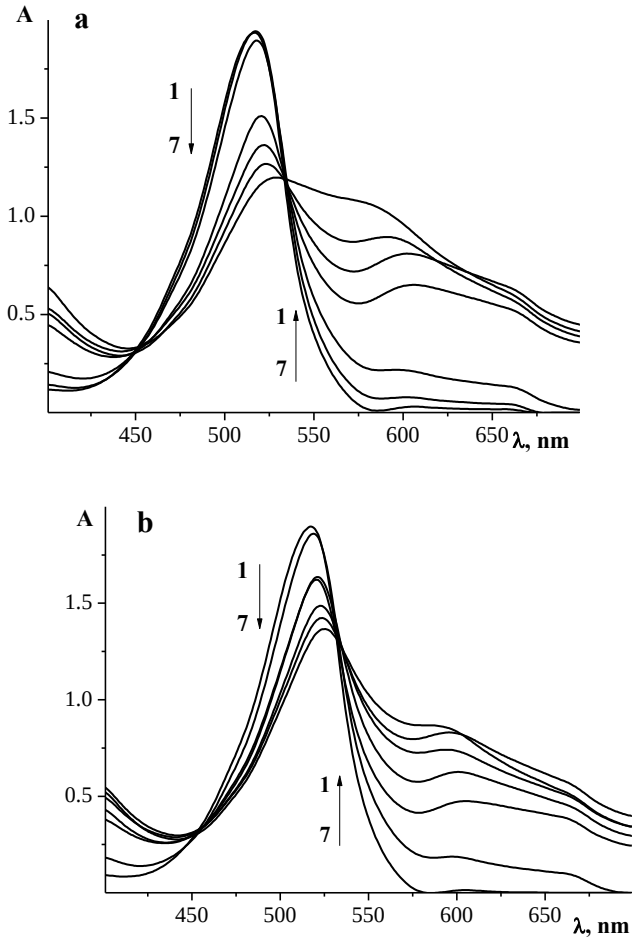

Figure 2. Rhodamine 6G absorption spectra in the presence of different quantities of mephenaminic (a) and phenylanthranilic (b) acids: 4×10^{-5} mol/l R6G; 1–7: 1×10^{-7}–2×10^{-4} mol/l Mef (Paa); at pH =9

3. RESULTS AND DISCUSSION

By mixing the dye with Mef and Paa, the systems' light-absorption characteristics are changed. By increasing the Mef or Paa concentrations, maintaining R6G content constant, the bathochromic adsorption band shift of the dye is observed (Fig. 2), which may confirm the IA formation. The appearance of an isosbestic point at 533 nm indicates the formation of the compounds with constant composition, and the reduction of the basic dye (BD) absorption maximum (by 25–30 %) with insignificant counter-ion concentrations (0.00005 mol/l), confirms the intensive R6G association with the analyte acids. The IA formation is also confirmed by the IR spectra, presented in Fig. 3.

If the diluted reagent solutions (avoiding dimerization) are used, and solution pH, for which the one-charged ions are more characteristic, is maintained, the IA formation may be described by the scheme:

$$Na^+An^- \leftrightarrow Na^+ + An^-, \quad (1)$$
$$Ct^+Cl^- \leftrightarrow Ct^+ + Cl^-, \quad (2)$$
$$Ct^+ + An^- \leftrightarrow Ct^+ \times An^-. \quad (3)$$

Therefore, the association constant will be equal to [32]:

$$K_{as} = \frac{\left[Ct^+ \times An^-\right]}{\left(C_{An^-} - \left[Ct^+ \times An^-\right]\right) \times \left(C_{Ct^+} - \left[Cn^+ \times An^-\right]\right)} \quad (4)$$

Herein Ct^+ is the R6G cation, An^- stands for analyte acid anion, C_{Ct+} and C_{An-} are general concentrations of R6G and Mef (Paa), $[Ct^+ \times An^-]$ is the IA equilibrium concentration, calculated as Eq. (5):

$$\left[Ct^+ \times An^-\right] = \frac{\varepsilon_{Ct} \times C_{Ct^+} \times l - A}{\left(\varepsilon_{Ct^+} - \varepsilon_{as}\right) \times l}, \quad (5)$$

Here A stands for the optical density of the solution in R6G cation maximal absorption, ε_{Ct} and ε_{as} stand for the correspondent coefficients of the molar absorption of the dye cation and analyte organic acid anion.

The association constants, calculated by the described manner are 2.5×10^{-4} and 2.0×10^{-3} for Mef and Paa IA correspondently.

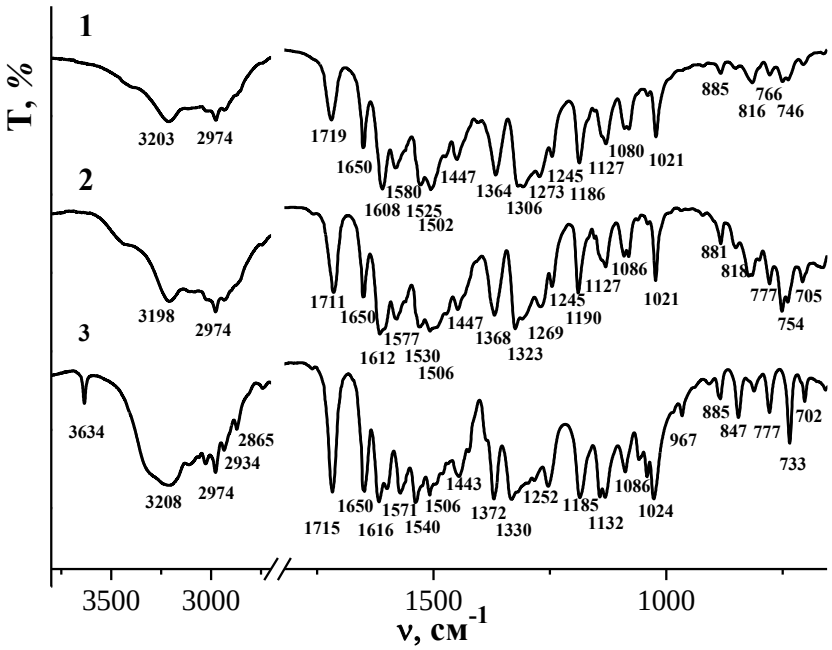

Figure 3. Absorption IR-spectra for ion associates of Phenylanthranilic (1) and Mepheminic acids (2) with R6G, and for the pure R6G (3)

Taking into account the low solubility of these compounds in water, the enhancement of the concentration of reagents leads to the IA suspension formation, permitting to yield it in solid-state.

$$Ct^+ + An^- \leftrightarrow Ct^+ \times An^- \downarrow \quad (6)$$

In order to evaluate quantitatively this biphase equilibrium, the solubility constant is used:

$$K_s = [Ct^+] \times [An^-]. \quad (7)$$

The solubility constant value is known to be one of the most important parameters for the viability of use of ionic compounds as electroactive compounds for ion-selective sensors [33]. The equilibrium concentration of the IA components is facile to detect spectrophotometrically after the IA deposition. The K_s values for analyte acids IA ($Mef^- \times R6G^+$) and ($Paa^- \times R6G^+$) are equal to 9.98×10^{-10} and 1.35×10^{-9} correspondently.

As at least three components with different properties and functions form the membrane composition, it's important to investigate the influence of the variation of the content of each one of them. The electroactive substance as the principal membrane component causes the response of the electrode to the analyte. PVC is used as an inert host matrix and gives strength to the matrix. The plastifiers not only give it jelly consistency but also serve as a solvent for

IA. The content of all of the mentioned components may alter strongly the ISE response. Therefore, the membrane composition has to be optimized.

In order to investigate the plastifier nature influence on the ISE basic characteristics, the similarly constructed membranes, plastified by DBS, DBP, DNF, DOP, and TCF were constructed. The plastifier content was 65 % of the general membrane weight. The measures were carried out at pH=9. The sensor response, depending on the plastifier nature is represented on Fig. 4. All of the electrodes have shown a hyper-Nernstian slope (70–95 mV/pC) and the sensitivity of $n \cdot 10^{-4}$ mol/l. The best characteristics were of DBP and TCF plastified ISE.

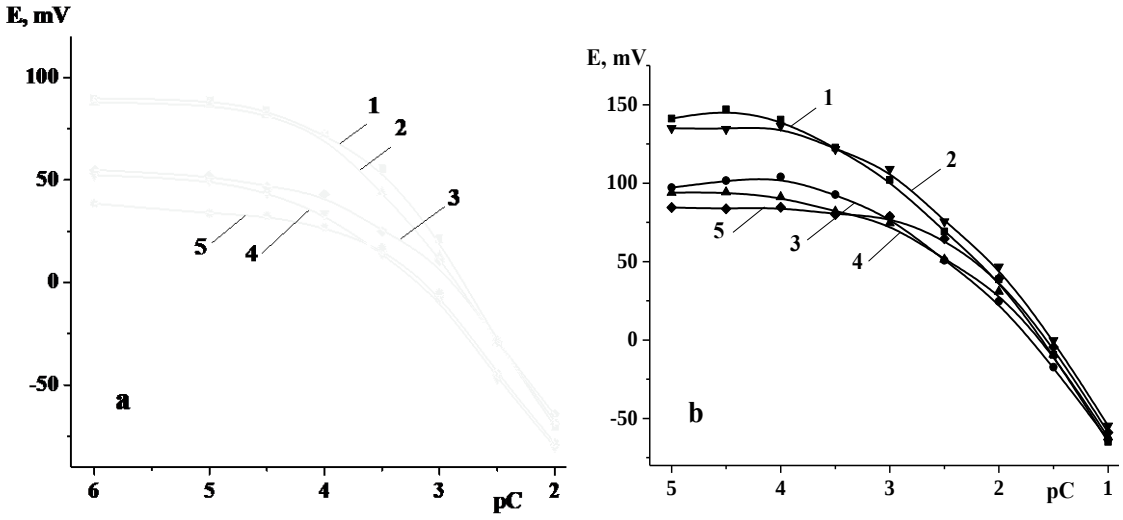

Figure 4. The plastifier nature influence on the response of the a) phenylanthranilate-selective electrode; b) mephenamate-selective electrode with plastifiers 1 – TCP; 2 – DBP; 3 – DNP; 4 – DBS; 5 – DOP

The deposited IA were used as EAS by producing ISE. The investigation of the electrochemical properties of the ISE with different EAS content (1–10 %) confirms their response to the analytes in vast concentration interval: $n \times 10^{-4}$–1×10^{-2} and $n \times 10^{-3}$–1×10^{-1} mol/l to Mef and Paa correspondently. The EAS content in the membrane with 4–8 % of EAS doesn't influence significantly to the sensors' electroanalytical characteristics (Table. 1). The further augmentation of the IA content leads to the thickening and hardening of the membrane and less sensitive slope and detection limit.

The significant influence on the electrode electroanalytical properties is given by the change of the plastifier content in the membrane. The investigations were carried out for the membranes with DBP content of 35 to 75 %. The best electroanalytical properties are characteristic for the electrode with a plastifier content of 45% to 70% (Table 1).

Table 1. The electroanalytical properties of the sensors

IA content, %	DBP, %	(MEF)(R6G)			(PAA)(R6G)		
		S, mV/pC	*a*, mol/l	C_{min}, mol/l	*S*, мВ/pC	*a*, mol/l	C_{min}, mol/l
2		94 ± 1.2	1×10^{-3}–1×10^{-2}	2.3×10^{-4}	89 ± 1.2	1×10^{-3}–1×10^{-2}	4.1×10^{-4}
4		94 ± 1.0	8×10^{-4}–1×10^{-2}	2.7×10^{-4}	87 ± 1.1	1×10^{-3}–1×10^{-2}	5.8×10^{-4}
6	65	83 ± 1.0	5×10^{-4}–1×10^{-2}	6.7×10^{-5}	89 ± 1.1	2×10^{-3}–1×10^{-2}	5.6×10^{-4}
8		87 ± 1.0	6×10^{-4}–1×10^{-2}	3.1×10^{-4}	81 ± 1.2	1×10^{-3}–1×10^{-2}	4.0×10^{-4}
10		74 ± 1.2	4×10^{-4}–1×10^{-2}	1.3×10^{-4}	84 ± 1.1	1×10^{-3}–1×10^{-2}	5.3×10^{-4}
6	35	69 ± 1.1	9×10^{-4}–1×10^{-2}	3.5×10^{-4}	73 ± 1.0	1×10^{-3}–1×10^{-2}	5.8×10^{-4}
	45	83 ± 1.2	7×10^{-4}–1×10^{-2}	3.2×10^{-4}	83 ± 1.1	1×10^{-3}–1×10^{-2}	4.8×10^{-4}
	55	90 ± 1.3	1×10^{-3}–1×10^{-2}	3.1×10^{-4}	84 ± 1.2	1×10^{-3}–1×10^{-2}	6.7×10^{-4}
	65	83 ± 1.0	5×10^{-4}–1×10^{-2}	6.7×10^{-5}	89 ± 1.1	2×10^{-3}–1×10^{-2}	5.6×10^{-4}
	70	85 ± 1.1	8×10^{-4}–1×10^{-2}	2.2×10^{-4}	85 ± 1.1	1×10^{-3}–1×10^{-2}	4.7×10^{-4}
	75	82 ± 1.2	4×10^{-4}–1×10^{-2}	1.4×10^{-4}	94 ± 1.1	2×10^{-3}–1×10^{-2}	5.6×10^{-4}

Other important factors, influencing the electrochemical properties of the sensors are the content and concentration of the electrode internal solution. The concentration change between 1×10^{-2} and 1×10^{-3} mol/l does not alter the main sensor characteristics. The working pH is correspondent to the interval 9<pH<11 (Fig. 5). The stable potential values are established during 5 to 10 sec. The membranes may be used for at least 4 months.

The selectivity of the investigated system gains special attention, as the selectivity of the potentiometric sensors still doesn't have a unique theoretical explanation. It is partially based on the specific connection between active centers and counter-ions. In order to estimate the interfering ion influence to the electrode potential, we use the Nikolski-Eisenmann equation [33]:

$$\Delta E = \Delta E^0 \pm \frac{R \cdot T}{z_m \cdot F} \ln\left[a_M + \sum_{a_S} K_{M-S} (a_s)^{z_m / z_s} \right] \qquad (8)$$

where $K_{M\text{-}S}$ stands for the selectivity coefficient.

The selectivity coefficient was detected according to IUPAC recommendations [34] by the separate solutions method. The data are joined in Table 2. The ISE is highly selective in the presence of F^-, Cl^-, Br^-, $S_2O_3^{2-}$, $C_6H_5COO^-$, BO_3^{3-} ions. Yet the iodides, salicylates, and picrates influence the selectivity much stronger. The mephenate-selective electrode is more selective than previously known [21] in the presence of Cl^--ions, which are very often to occur in investigated objects.

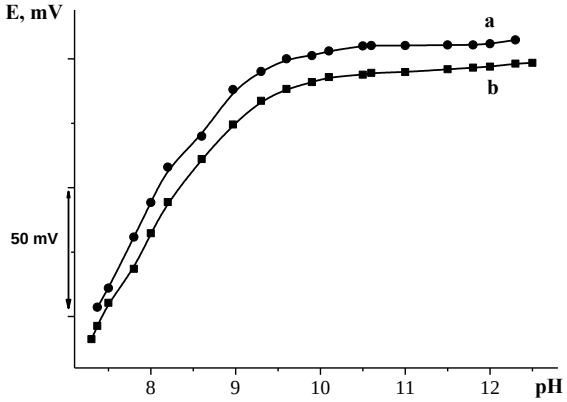

Figure 5. The pH-dependence of the sensors, based on IA (Mef^-)($R6G^+$) (a) and (Paa^-)($R6G^+$) (b)

Table 2. Selectivity coefficient of the developed and known Mef-selective sensors

Ion	$-\lg K^{пот}_{i,j}$		
	Membrane ($R6G^+$)(Mef^-) ISE	Membrane ($R6G^+$)(Paa^-) ISE	Mercury(I) Mef ISE [21]
Cl^-	4.75	4.8	0.52
Br^-	4.50	4.0	-
I^-	2.63	2.68	-
F^-	4.82	4.66	-
SCN^-	2.08	1.55	-
ClO_4^-	1.35	1.02	-
SO_4^{2-}	> 5	> 5	4.42
Sulfanol	0.72	1.02	
Oxalate	> 4	> 4	2.55
Tartrate	> 4	> 4	2.68
Benzoate	4.16	3.27	2.54
Picrate	1.09	1.05	-
Phthalate	> 4	> 4	2.52
Salicylate	2.74	2.92	2.49

The approbation of the sensors, developed in this work, was made by the method of "added and found" (Table 3) for Paa and by comparison of Mef content in pharmaceutical preparations

with preparation certificates (Tabl. 4). Parallelly, the determination of these substances was carried out by biphase titration with an alkali [28].

3.1. The mefenamic and phenanthranilic acid determination techniques

The capsules and pills are previously melted in the mortar and then dissolved in distilled water and filters, in order to separate the solid particles. The filtrate is put into the 50 mL beaker, where 5 ml of universal pH=9 buffer solution is added. The solution is diluted by the water to the mark.

Table 3. The mefenamic and phenanthranilic acid determination in solution by sensors and biphase titration (n=3; P=0.95)

Determination technique	IA-based sensor with R6G [this work]		Biphase titration [28]	
Determined component	Mef	Paa	Mef	Paa
Added, mg	50.0	100.0	50.0	100
Found, x ± Δx mg	50.4 ± 0.9	100.9 ±1.5	57.7 ± 2.6	102.7 ± 1.3
S^2	1.22	1.49	1.92	0.49
RSD (*Sr*,x %)	0.81	1.20	1.06	0.30
Technique confirmation:	Mef		Paa	
F-test (F_{th} = 5.05)	1.57		3.04	
t–test (t_{th} =1.87)	1.04		0.79	

The electrodes are put to a cup with the solution and measure the electrode potential. The concentration of the analytes is found by their calibration curves, developed in analogous conditions with the known concentration standard solutions.

Table 4. Mefenamic acid determination in pharmaceutical formulation (n=3; P=0.95)

Pharmaceutical formulation	Registered content	Found, mg	S^2	*RSD* (*Sr*, x %)
"Flamingo" capsules, India	250 mg	250.5 ± 2.7	1.15	0.43
"Darnytsia" pills, Ukraine	500 mg	500.3 ± 2.2	0.75	0.17
"Ananta" capsules, United Kingdom	500 mg	500.1 ± 2.9	1.42	0.24

The main electroanalytical characteristics of the sensors and their comparison with the known Mef sensor are represented in Table 5.

Table 5. The comparison of the electroanalytical mefenamic and phenantranilic acid sensors

ISE Electroanalytical characteristics	IA-based sensor ($R6G^+$)(Mef^-)	IA-based sensor ($R6G^+$)(Paa^-)	Mercury (I) Mefenamic ISE [21]
Working solution pH	9.0–11.0	9–11	6.0–9.0
Electrode function slope mV/pC	83.1 ± 1.0	89.1 ± 1.1	64.6 ± 1.5
Linearity, mol/l	5×10^{-4}–1×10^{-2}	2×10^{-3}–1×10^{-1}	1.0×10^{-6}–1.0×10^{-2}
Sensitivity, mol/l	1.8×10^{-4}	5.6×10^{-4}	6.2×10^{-7}
Response time, s	10	10	25

4. CONCLUSION

The issues of quality control of pharmaceutical products remain relevant to modern analytical chemistry. This is due to an increase in the number of registered pharmacopeia medicines (often different manufacturers) and the introduction of pharmaceutical practices of high-level substances belonging to the new classes of natural and synthetic compounds, and economic changes in the pharmaceutical market through the introduction of the scope of treatment at the international and regional levels of various substances in addition to ready-made drugs. The most essential are the techniques that allow expressive determination of substances in pharmaceutical preparations without prior separation or concentration.

Mefenamic acid (Mef) is a derivative of phenylanthranilic acid (Paa). As a drug of the NSAID group, it reduces the sensation of pain and suppresses the development of inflammation in the human body. But an important advantage over other drugs in this group is the immunostimulating and antipyretic effect, due to which Mef is often used in medical practice.

The developed mefenamic and phenilanthranilic sensors are characterized by sensitive electrode function slope and efficient function in alkaline media. The important electrode advantages are their rapidity in potential establishment and high selectivity to the interfering ions.

REFERENCES

[1] State Pharmacopoeia of Ukraine, Kh.: State Enterprise "Scientific-Expert Pharmacopoeia Center" (2004).

[2] C. V. Winder, J. Wax, L. Scotti, R. A. Scherrer, E. M. Jones and F. W. Short, J. Pharmacol. Exp. Ther. 138 (1962) 405.

[3] N. G. Voytenko, Ukr. Med. Journ.81 (2011) 75.
[4] European Pharmacopoeia. 5th Ed. Strasbourg (2005) 1984.
[5] British Pharmacopoeia 2009, London (2009) 9335.
[6] Unated States Farmacopea National Formulary, USP 26, NF21-Rockville (2003) 1142 .
[7] K. Hoshina, S. Horiyama, H. Matsunaga and J. Haginaka, Pharm. Biomed. Anal. 55 (2011) 922.
[8] N. Jagota, and J. Stewart, J. Chromatogr. 604 (1992) 255.
[9] M. R. Rouini, A. Asadipour, Y. H. Ardakani, and F. Aghdasi, J. Chromatogr. B 800 (2004) 189.
[10] Y. Sun, K. Takaba, H. Kido, M. N. Nakashima, and K. Nakashima, J. Pharm. Biomed Anal. 30 (2003) 1619 .
[11] A. Raza, J. Analyt. Chem. 63 (2008) 244 .
[12] N. A. Alarfaj, S. A. Altamini, and L. Z. Almarshady, Asian J. Chem. 21 (2009) 216.
[13] S. Zommer-Urba?ska, and H. Bojarowicz, J. Pharm. Biomed. Anal. 4 (1986) 481.
[14] N. S. Othman, and L. S. Awadis, J. Raf. Sci. 20 (2009) 8.
[15] C. Roosewelt, N. Harihrishnan., V. S. Gunasekaran, S. Chandrasekaran, V. Haribaskar, and B. Prathap, Asian J. Chem. 22 (2010) 843.
[16] A. Aboul Khier, M. El Sadek, and M. Baraka, Analyst. 112 (1987) 1399 .
[17] I. Zseltvay, O. Zheltvay, and V. Antonovich, Acta Pol. Pharm. 68 (2011) 629.
[18] C. S. Sastry, A. S. Prasad Tipirneni, and M. V. Suryanarayana, Analyst 114 (1989) 513.
[19] S. O. Idowu, S. C. Tambo, A. O. Adegoke, and A. A. Olaniyi, Tropical J. Pharm. Research. 1 (2002) 15.
[20] A. S. Issa, Y. A. Beltagy, M. H. Gabr Kassem, and G. Daabees, Talanta 32 (1985) 209 .
[21] A. O. Santini, H. R. Pezza, and L. Pezza, Sens. Acurators B 128 (2007) 117 .
[22] O. Cakirer, E. Kilie, O. Atkol, and A. Kenar, J. Pharm. Biomed. Anal. 20 (1999) 19 .
[23] L. Liu, and J. Song, Anal. Biochem. 354 (2006) 22 .
[24] J. F. Song, W. Guo, X. F. Kang, and H. Yin Hua, Science in China. Series B, Chemistry, Life sciences & Earth sciences 36 (1993) 906.
[25] M. Y. Khuhawar, T. M. Jehangir, and F. M. A. Rind, J. Chem. Soc. Pakistan 23 (2001) 226 .
[26] S. Husain, M. Kifayatullah, and R. Sekar, Indian J. Chem. Technol. 8 (2001) 191.
[27] P. O. Bezugliy, Pharmaceutical Chemistry: Teaching. manual for the stud. higher pharmacy teach shut up. Kh: NFAU (2002).
[28] N. P. Kobzar, S. G. Isaev, and O. M. Svechnikova J. Org. and Farm. Chem. 4 (2006) 70.
[29] Z. Kormosh, I. P. Hunka, and Y. R. Basel, Chemical Series 15 (2007) 99.
[30] Z. Kormosh, I. Hunka, and Y. Bazel, Chin. Chem. Lett. 18 (2007) 1103.
[31] K. Kamman, Work with ion-selective electrodes: Mir, Moscow (1980).
[32] S. A. Shapovalov, Russian Journal of Physical Chemistry A. 85 (2011) 1369.

[33] V. Morf, Principles of robots of ion-selective electrodes and membrane transport: Transl. from English. Mir, Moscow (1985).
[34] Y. Umezawa, K. Umezawa, and H. Sato, Pure Appl. Chem. 67 (1995) 507.

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