UDC 543.6

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EFFECT OF PLASTICIZER ON THE CHARACTERISTICS OF MOLECULARLY IMPRINTED POLYMER BASED POTENTIOMETRIC SENSOR FOR PROPRANOLOL

The effect of different plasticizers on the performance and selectivity coefficient of molecularly imprinted polymer (MIP) based potentiometric sensor in mixed non-aqueous mediums was first investigated. The research was undertaken for propanolol imprinted MIP. Plasticizers (di-n-octyl phthalate (DOP), dibutyl phthalate (DBP) and dioctyl sebacate (DOS)) were used in MIP based sensors for potentiometric determination of propranolol, as well as to change the resistance of the sensing polyvinylchloride membrane and to improve the detection limit and selectivity of the electrodes. For propranolol-selective sensors, the nature of plasticizer influences distribution of MIP particles in polyvinylchloride, slope of electrode function, linear range and selectivity coefficients. The applicability of the proposed sensors was tested by potentiometric propranolol determination in aqueous modeling solution with the use of tablets of pharmaceutical formulation.

Keywords: Plasticizer; Molecular imprinted polymer; Propranolol; Potentiometric sensor; MIP-based sensor; MIP microspheres.

Introduction. Potentiometric sensors based on ion-selective electrodes have certain advantages among different kinds of sensors that may be used in arrays. Among those are rapid response, reproducibility, and simplicity of the measuring technique [1]. This group of chemical sensors is also characterized as simple in preparation, robust in operation and moderately selective in analytical performance [2]. Introduction of polyvinylchloride matrix and realization of the membrane in the form of doped organic gel was a significant turning point in the development of potentiometric sensors [3].

Polyvinylchloride (PVC) is an amorphous and naturally rigid polymer [4]. When mixed with a plasticizer (low-molar mass additive), however, this polymer becomes flexible with appropriate chemical and physical characteristics [5; 6]. When a plasticizer is added, the free volume of the polymeric chain is expanded, making penetration of an analyte easier, increasing its interaction with the sensing phase. Plasticizer ensures the mobility of the free and complexed ionophore, sets the dielectric constant, and provides suitable mechanical properties of the membrane [7]. There are many plasticizers used for preparation of plasticized PVC films: phthalates, sebacates, ortho-nitrophenyl octyl ether (NPOE), etc.

Molecularly imprinted polymer (MIP) or ion imprinted particles can be used as electro-active substances of potentiometric sensors with specific binding for an analyte [8] and can be incorporated into the polyvinylchloride matrix by mixing the particles with appropriate plasticizer. PVC membranes thus prepared were used for potentiometric sensing, with targets such as uranium (VI) [9], dysprosium (III) [10], copper (II) [11], atrazine [12], chlormequat [13], tetracycline [14], chlortetracycline [15], oxytetracycline [16], doxycycline [17], amoxicillin [18], ciprofloxacin [19], promethazine [20], chlorpromazine [21], levamisole hydrochloride [22], sertraline [23], lamotrigine [24], melamine [25], norfloxacin [26], methylphosphonic acid [27], pinacolyl

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methylphosphonate [28], dietyl chlorophosphate [29], phorate [30], clenbuterol [31] and myoglobin [32].

Dissociation constants in ion-selective membranes are dominated by the dielectric constant of membranes. The simplest way to change the dielectric properties of PVC membranes is by changing the membrane plasticizer [33]. So an appropriate choice of plasticizer is essential to obtain desirable characteristics of a PVC film that can be used as a sensing phase [34]. Effect of different plasticizers on the sensitivity and linearity (however, not selectivity) of MIP based potentiometric sensors was investigated in some papers [12; 22; 27; 29]. The membrane with DOP and bis(2ethylhexyl) sebacate (BENS) offered better linear response for atrazine sensors then NPOE and tris(2ethylhexyl)phosphate (TEHP) [12]. Among 5 different plasticizers employed, NPOE, benzyl acetate (BA), sebacic acid dibutyl ether (DBS), DOP and dioctylphenyl phosphonate (DOPP), the plasticized membrane of levamisole sensors with DBS appeared to be more compatible with the MIP [22]. The sensitivity of metilphosphonic acid sensors can be directly related to dielectric constant of plasticizer [27]. Membrane with NPOE offer better potential responses of dietyl chlorophosphate sensors in the entire concentration range of diethyl chlorophosphate (DCP) compared to TEHP, DOP and BEHS based sensors [29].

The present study deals with MIP potentiometric sensors of propanolol based on polyvinylchloride. The aim was to evaluate the effect of plasticizers on sensor's sensitivity, selectivity and possibility of application in mixed and non-aqueous medium.

Experimental

Reagents. (*R*,*S*)-Propranolol hydrochloride (99%) was obtained from Fluka (Dorset, UK). Methacrylic acid (MAA, 98.5%) was purchased from ACROS (Geel, Belgium) and used as received. Divinylbenzene (DVB, technical grade, 55%, mixture of 1,2-, 1,3- and 1,4-isomers) and trimethylolpropane trimethacrylate (TRIM, technical grade) were obtained from Aldrich (Dorset, UK). Prior to use, DVB was passed through an aluminum oxide column to remove the polymerization inhibitor. Acetic acid (glacial, 100%), acetonitrile (99.7%) and azobisisobutyronitrile (AIBN, 98%) used for polymer synthesis were purchased from Merck (Darmstadt, Germany). AIBN was re-crystallized from methanol before use. High molecular mass poly(vinyl chloride) (PVC), di-n-octyl phthalate (DOP), dibutyl phthalate (DBP), dioctyl sebacate (DOS), metoprolol tartrate salt, atenolol were purchased from Sigma-Aldrich. All other chemicals and solvents were of analytical grade.

Stock standard solution (0.1M) of propranolol hydrochloride was obtained by dissolving 1.479 g propranolol hydrochloride in 50 mL of water. Standard solutions of propranolol hydrochloride (1.0×10^{-2} to 1.0×10^{-8} M) were prepared by serial dilution of the stock solution by deionized water.

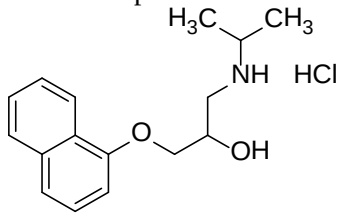
Stock standard solutions (0.1M) of propranolol hydrochloride in acetonitrile/citrate buffer pH 6.0 (50/50%, v/v) (ethanol/citrate buffer pH 6.0 (20/80%, v/v) or 0.1 M $NaNO_3$) were obtained by dissolving 1.479 g propranolol hydrochloride in 50 mL of corresponded solvent. Standard solutions of propranolol hydrochloride (1.0×10^{-2} to 1.0×10^{-8} M) were prepared by serial dilution of the stock solution by acetonitrile/citrate buffer pH 6.0 (50/50%, v/v) (ethanol/citrate buffer pH 6.0 (20/80%, v/v) or 0.1 M $NaNO_3$ respectively).

Preparation of propranolol-imprinted and non-imprinted particles. Molecularly imprinted microspheres with the average diameter 1.8 μm were synthesized using precipitation polymerization reported in [35]. The template molecule, (*R*,*S*)-propranolol

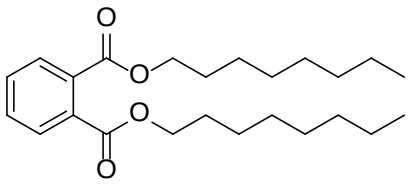
was dissolved in 40mL of acetonitrile in a 150mm×25mm borosilicate glass tube equipped with a screw cap. The functional monomer (methacrylic acid), the cross-linking monomer (divinylbenzene and trimethylolpropane trimethacrylate) and the initiator (azobisisobutyronitrile) were then added. The solution was purged with a gentle flow of Ar for 5 min and sealed under Ar. Polymerization was carried out by inserting the borosilicate glass tube fixed horizontally in a Stovall HO-10 Hybridization Oven (Greensboro, NC, USA), and rotated at a speed of 20 rpm. The temperature was ramped from 20^0C to 60^0C within 20 min, thereafter kept for 24 h. After polymerization, particles were collected by centrifugation. The template was removed by batch mode solvent extraction with methanol containing 10% acetic acid (v/v), until no template could be detected from the washing solvent by spectrometric measurement. Polymer particles were finally washed with acetone and dried in a vacuum chamber. Non-imprinted reference polymers were synthesized under identical conditions except for omission of the template (*R*,*S*)- propranolol.

Membrane preparation and electrode construction. Sensor membranes were fabricated by following the general procedure reported at [36]. Propranolol imprinted and non-imprinted particles (20 mg) were dispersed in 0.2 mL of DOP (DBP or DOS) (fig.1) and homogenized in a sonicator. A solution of 200 mg of PVC in 4 mL cyclohexanone was added and the mixture was intensively stirred for 10-15 min at 50-60°C to form a homogeneous mass. The resulting solution was poured in a 37 mm Petri dish and kept at room temperature to remove the solvent. Blank membranes were prepared in a similar way except for omission of the molecularly imprinted and non-imprinted microspheres.

The polymer membranes thus obtained were elastic films, from which disks with a diameter of 10 mm were cut out and glued to the one end of PVC tube with cyclohexanone. The tube was filled with an internal solution of 10^{-3} M propranolol hydrochloride. The potentiometric sensors were kept in air when not in use.



Propranolol hydrochloride



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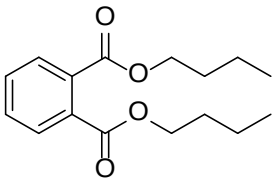
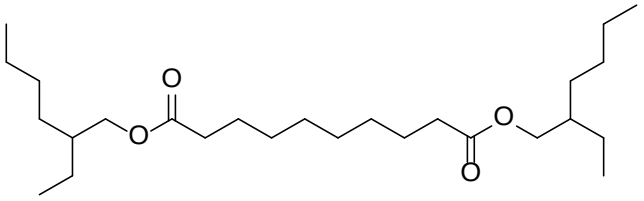


Dibutyl phthalate



Dioctylsebacate

Fig. 1. The chemical structure of propranolol and plasticizers

The response of the sensor was evaluated by measuring the electromotive force (EMF) of the following electrochemical cell: Ag, AgCl, 10^{-3} M propranolol hydrochloride | Electrode membrane | Sample solution | Saturated KCl, AgCl, Ag. The EMF measurements were carried out at room temperature with an EV-74 potentiometer (Russia). The potential response of each sensor for the sample solution containing propranolol hydrochloride in interval from 1.0×10^{-2} to 1.0×10^{-8} M) was measured and plotted as a function of analyte concentration.

Analytical determination. 1. Propranolol determination in modeling solutions. Samples with known amounts of propranolol hydrochloride were analyzed by following the analytical procedure described above. The amount of propranolol hydrochloride was determined using calibration curve method.

2. Propranolol determination in pharmaceutical formulation "Anapriline-Zdorov'e" (Kharkiv, Ukraine, 40 mg of propranolol hydrochloride in 1 tablet). 5 tablets of formulation were dissolved in 30 mL of water under stirring conditions and transferred into a 50 mL volumetric flask, 5 mL of pH 6.0 citrate buffer solution was added and completed to volume with water. Aliquots of 0.54 mL, 1.78 mL, 12.5 mL of the sample solution were diluted to 25 mL with water. The potentiometric propranolol-selective sensor and the reference electrode were immersed into the test solutions and EMF reading was recorded. The amount of propranolol hydrochloride was determined using the calibration curve method.

Results and discussions

The synthesized MIP microspheres for propranolol were incorporated into the PVC membrane and tested as a sensing material in the proposed potentiometric sensor. One of the variables involved in the optimization of the sensor characteristics and MIP compatibility with PVC was the nature of plasticizer. For our research we have chosen 3 commonly used plasticizers - di-n-octyl phthalate, dibutyl phthalate and dioctyl sebacate.

Distribution of MIP particles in polyvinyl chloride membrane. The study of a membrane matrix can give information about distribution of an ion exchanger in the membrane. The most readily available technique for estimating a change in the structure of polymer matrix is studying the surface morphology of polyvinylchloride film membranes [37]. Morphology of the polyvinylchloride membrane surface of MIP-based potentiometric sesnors was studied with regard to the nature of used plasticizer (Fig. 2). It was found that DOP gives the best distribution of MIP particles compared to the other plasticizers. It is obvious that there are some undistributed MIP particles in polyvinylchloride membrane plasticized by DBP. In case of DOS there were many aggregates at the top surface of the PVC polymer membrane.

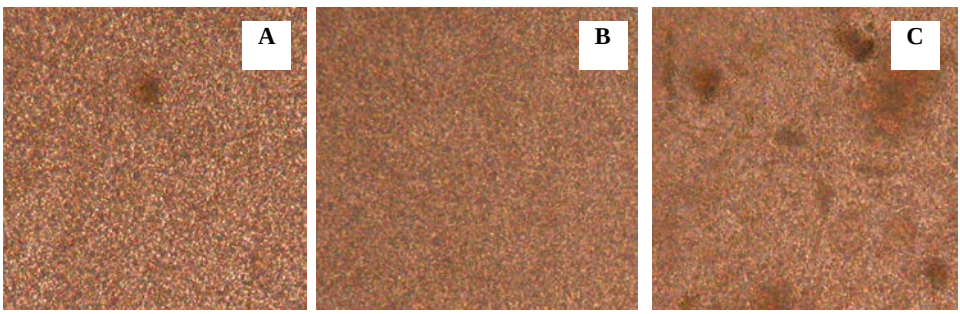


Fig. 2. Influence of plasticizer on MIP particles distribution in polyvinylchloride membrane (100×). A – DBP; B – DOP; C – DOS

Response characteristics of the electrodes. The performances of sensors prepared with one of three plasticizers were experimentally compared. The results and calibration graphs obtained with three sensors are shown in Table 1 and Figure 3A.

From the Table 1 and Figure 3A, it is obvious that the sensors with DBS and DOS exhibit good potential responses in aqueous solution of propranolol hydrochloride: linearity range of 10^{-1} - 10^{-5} M and 10^{-1} - 10^{-6} M respectively. It is over 1 or 2 orders of magnitude better than sensor with the use of DOP as plasticizer of PVC membrane. The most sensible value of slope corresponds to the sensor constructed by using DOP as

plasticizer. As can be seen from Table 1, obtained correlation coefficients testify to a good linearity of calibration curves for each plasticizer used as a solvent mediator in this study. The slopes of sensors obtained in propranolol solutions in the range 10^{-1} - 10^{-4} M have the order DBP < DOP < DOS that can be correlated to the lipophilicity of the solvents: 4.45 < 7.0 < 10.1, respectively or dielectric constants: 6.4 > 5.1 > 3.9, respectively.

Table 1

Response characteristics of the propranolol-selective electrodes

Parameter	Plasticizer of the electrode		
	DOP	DBP	DOS
Slope (mV dec^{-1})	53.5	51.5	51.6
Linearity range, M	10^{-1} - 10^{-4}	10^{-1} - 10^{-5}	10^{-1} - 10^{-6}
Detection limit, M	10^{-4}	10^{-5}	10^{-6}
Equation	y = -53.5x + 330.5	y = -51.5x + 338.5	y = -51.6x + 337.9
Correlation	0.9974	0.9976	0.9925

Sensors response in background electrolyte and non-aqueous media. The effect of different plasticizers on the performance of MIP based potentiometric sensors in background electrolyte and mixed non-aqueous mediums was first investigated. The performance of electrodes with different plasticizers in 0.1 M $NaNO_3$ background solution and partially non-aqueous media using acetonitrile – water and ethanol-water mixtures were assed and results obtained are shown in Figure 3 and presented in Table 2. As seen from the Table 2 the nature of plasticizer plays a significant role in the slope and linearity range of MIP-based sensors for propranolol in different aqueous and partially non-aqueous mixed media, but the main changes in electrode performance can be seen for the aqueous media (Figure 3). The presence of $NaNO_3$ decreases the slope of all sensors but in case of DOS used as plasticizer the change is less than for the other 2 sensors with the use of DBP and DOP as plasticizers.

Table 2

Response characteristics of the propranolol-selective electrodes in different medium

Electrode plasticizer	Water		Acetonitrile (50%)		Ethanole (20%)		Ethanole (50%)		0.1 M $NaNO_3$	
	pC	S, mV dec^{-1}	pC	S, mV dec^{-1}	pC	S, mV dec^{-1}	pC	S, mV dec^{-1}	pC	S, mV dec^{-1}
DBP	1-4 1-5	53.0 51.5	1-4	32.0	1-4 1-5	48.3 41.8			1-4 1-5	48.3 40.3
DOP	1-4	53.3	1-4	37.0	1-4	43.5			1-4 1-5	47.3 40.0
DOS	1-4 1-5 1-6	54.3 55.1 51.6	1-4	43.7	1-4 1-5	49.6 45.5	1-4 1-5	43.6 35.5	1-4 1-5	52.0 47.5

It was observed that in the presence of acetonitrile the slope of all sensors decreases remarkably and in opposite to the other medium sensors shows a stable potential in the concentration of propranolol hydrochloride in the range from 1.0×10^{-4} M to 1.0×10^{-7} M, that could be helpful in analysis of samples with unknown content of propranolol hydrochloride.

The slope of sensors is acceptable in the presence of ethanol up to about 20% (v/v) in the water and for the higher percentage of ethanol up to 50% (v/v), the slope decreases. The slopes obtained in acetonitrile show the largest changes in the following order DBP < DOP < DOS that can be correlated to the lipophilicity or dielectric constant of solvent mediator. MIP-based sensor prepared by using DOS as a membrane plasticizer showed the best response and can be used for estimation of propranolol hydrochloride in mixed non-aqueous solutions.

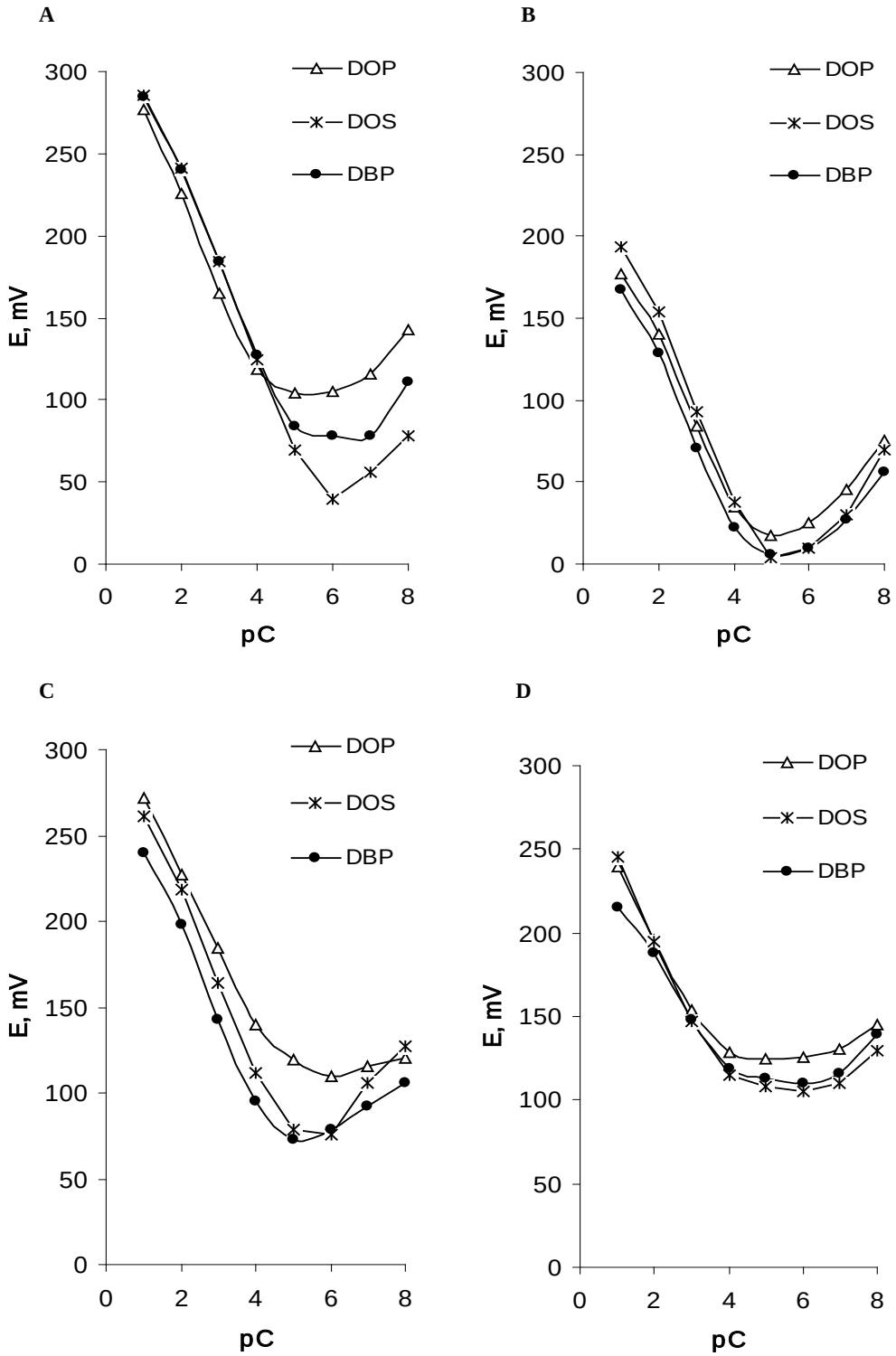


Fig. 3. Effect of plasticizer nature on the potentiometric response of propranolol sensors in water and mixed solutions. A – water, B – 0.1M $NaNO_3$, C – ethanol/citric buffer (20/80 v/v), D – acetonitrile/citric buffer (50/50 v/v)

The lifetime of the synthesized membranes is more then 9 months. The slope of MIP-based potentiometric sensors for propranolol decreases a little after 3 months of using in comparison to the new one (Table 2). The membranes with DBP, DOP and DOS offered high sensitivity to propranolol hydrochloride with the response of 52.0; 43.9 and 51.2 and mVdecade^{-1} over the range 10^{-1} - 10^{-4} M in water solution after 110-120 measurements respectively.

Sensitivity. The potential response of propranolol imprinted, non-imprinted polymer and blank membrane sensors fabricated under the same conditions, except for different type of plasticizer, was tested in water solution. Results obtained are shown in Fig. 4.

The observed potential response of blank membranes may be attributed to interaction of plasticizer with analyte or with H^+, as it was shown for blank membrane containing DOS as a plasticizer in [38]. As can be seen in the figure, the electrodes with different nature of plasticizer have significantly different potentiometric response. The electrodes with DOP as plastisizer have almost the same response for blank, NIP and MIP sensors (Fig. 4A) and the difference between blank and MIP membrane could be seen only in diluted solutions of propranolol with concentration less then 1.0×10^{-6} M. In case of DOS the difference in the potentiometric response of blank polymer membrane and NIP or MIP-based membranes could be clearly seen from the Fig. 4B. The plot obtained for the propranolol imprinted polymer membrane offers linear response in the ranges from 1.0×10^{-6} M to 1.0×10^{-1} M. Blank membrane has linear range to 1.0×10^{-4} M and in much diluted solutions has reversed function. The most significant imprinting effect could be seen for the electrodes containing DBP as a plasticizer (Fig. 4C). MIP based membrane gave a linear response for propranolol in the range from 1.0×10^{-5} M to 1.0×10^{-1} M and has no response changes in the range of propranolol concentrations from 1.0×10^{-5} M to 1.0×10^{-7} M. On the other hand, blank and NIP polymer has response in the diluted solutions of propranolol that could give mistakes in analytical applications and determination of propranolol concentration.

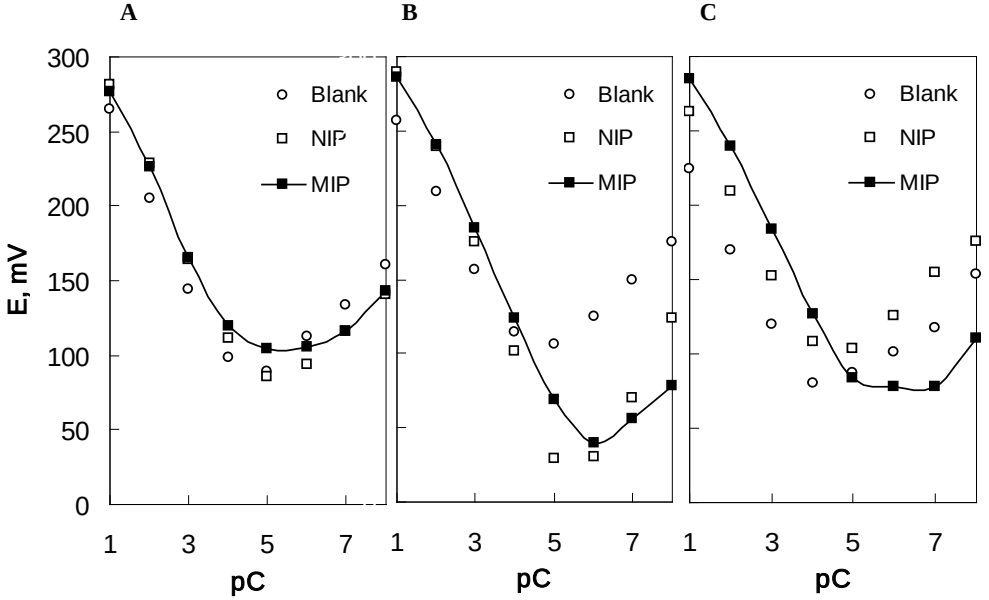


Fig. 4. Potential response of propranolol imprinted, non-imprinted and blank membrane potentiometric sensors with different plasticizers respect to propranonlol hydrochloride concentration (A - DOP, B - DOS, C - DBP)

Selectivity of the electrodes. The nature of a plasticizer or membrane solvent greatly affects all the electrochemical characteristics including potentiometric selectivity. Plasticizer influences both dielectric constant of the membrane and mobility of a molecule or ion in the membrane [22]. The effect of different plasticizers on the selectivity of MIP based potentiometric sensor was first investigated. The selectivity coefficients ($K^{pot}_{propranolol}$) of the proposed sensors with DOP, DOS and DBP as plasticizers toward different inorganic species and structural analogs were evaluated by a separation solution method. The values of selectivity coefficients calculated by this method are shown in Table 3 and Figure 5. From the data, it is obvious that the interfering inorganic species could not affect the selectivity of the proposed sensors towards propranolol hydrochloride. For sensors with plasticizers the interference of inorganic species and structural analogues increases in the order DOP < DOS < DBP that could be probably explained by a synergism [39] of dielectric constant and lipophilicity of the solvents. The sensor with DBP showed the best selectivity towards inorganic species and also structural analogues.

Table 3

Selectivity coefficients of the MIP-based electrodes with different plasticizer

Interfering species	$K^{pot}_{propranolol}$		
	DOP	DOS	DBP
KCl	2.1×10^{-1}	1.1×10^{-1}	3.0×10^{-2}
NH_4Cl	2.1×10^{-1}	5.7×10^{-2}	2.2×10^{-2}
NaAc	1.1×10^{-1}	4.1×10^{-2}	1.4×10^{-2}
$NaNO_3$	4.8×10^{-1}	3.7×10^{-2}	2.4×10^{-2}
$MgSO_4$	1.3×10^{-2}	4.6×10^{-3}	1.8×10^{-3}
$Ca(NO_3)_2$	1.2×10^{-2}	1.0×10^{-2}	5.5×10^{-3}
Urea	2.3×10^{-2}	8.8×10^{-3}	5.5×10^{-3}
Metoprolol tartrate	7.7×10^{-1}	1.4×10^{-1}	5.8×10^{-2}
Atenolol	2.6×10^{-1}	8.4×10^{-3}	1.3×10^{-2}

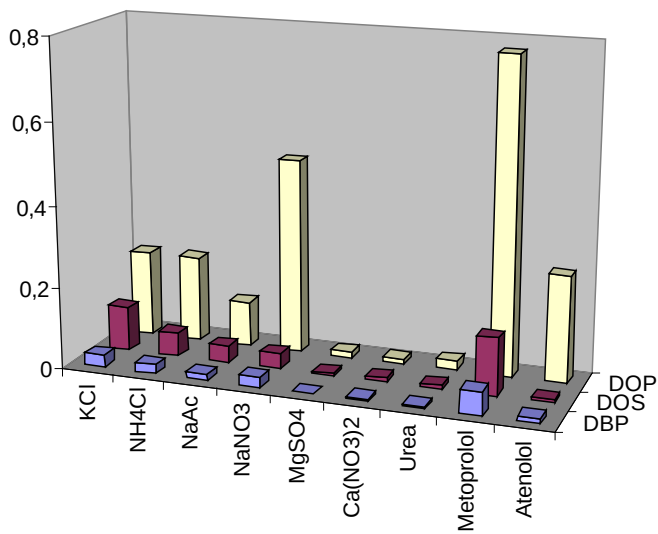


Fig. 5. Selectivity coefficients obtained for the MIP-based sensors for propranolol by using a separation solution method

Analytical application. Reliability of the proposed MIP based potentiometric sensors for quantification of propranolol was assessed by determining $2.9 \times 10^{-4} \sim 6.8 \times 10^{-3}$M propranolol solution using the calibration curve method. The results are shown in Table 4. In all cases the relative standard deviation was < 0.05. Propranolol was also determined in drug "Anapriline-Zdorov'e" (Ukraine) with good recovery, calculated from the nominal value (Table 4).

Table 4

Results of propranolol determination in modeling solutions and drug (n = 5, P = 0.95)

Sample	Composition of sensor membrane	Nominal value, $c \times 10^3$ M	Experimental value, $c \times 10^3$ M	S_r
Modeling solution	MIP - DOP	0.96	0.94±0.03	0.03
		6.75	6.75±0.20	0.02
	MIP – DOS	0.96	1.03±0.05	0.04
		6.75	5.85±1.60	0.20
Drug "Anapriline-Zdorov'e"	MIP - DOP	0.96	0.88±0.07	0.07
	MIP - DBP	0.29	0.30±0.05	0.13
	MIP - DOS	0.29	0.26±0.04	0.12

Conclusions. MIP-based sensors for propranolol were constructed by using DOP, DBP and DOS as plasticizers. These sensors showed a linear response with the slope close to Nernstian in the range 1.0×10^{-1} - 1.0×10^{-4}M and had practical detection limit within the range 10^{-4} to 10^{-6} M, respectively. The selectivity and effect of different plasticizers on the performance of MIP-based potentiometric sensors in background electrolyte, mixed non- aqueous mediums were first investigated. MIP-based sensor constructed by using DOS as plasticizer showed the best response in mixed non-aqueous media. The MIP-based sensor with DBP as plasticizer showed the best selectivity towards inorganic species and also structural analogues such as atenolol and metoprolol. The effects of plasticizer, mixed medium and background electrolyte on the potentiometric response of MIP-based sensors are primarily due to their influence on migration, ion-pair formation, and diffusion coefficients. So the nature of plasticizer has to be taken into account when developing MIP-based to achieve optimal sensitivity, selectivity, detection limit and applicability in mixed media.

Acknowledgements. The authors would like to acknowledge Swedish Institute (Visby Short-term research visit program, 2011) and Ukrainian Government (Program of International internships, 2012) for the financial support.

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ВЛИЯНИЕ ПЛАСТИФИКАТОРА НА ХАРАКТЕРИСТИКИ ПОТЕНЦИОМЕТРИЧЕСКОГО СЕНСОРА НА ОСНОВЕ ПОЛИМЕРА С МОЛЕКУЛЯРНЫМИ ОТПЕЧАТКАМИ ОБРАТИМОГО К ПРОПРАНОЛОЛУ

Впервые исследовано влияние различных пластификаторов на отклик потенциометрических сенсоров на основе полимеров с молекулярными отпечатками пропранолола в смешанных неводных средах и на коэффициент селективности разработанных сенсоров. Пластификаторы (ди-N-октилфталат (ДОФ), дибутилфталат (ДБФ) и диоктилсебацинат (ДОС)) были использованы в сенсорах на основе молекулярно-импринтированных полимеров (МИП) для изменения свойств поливинилхлоридной мембраны, улучшения предела обнаружения и селективности электродов при потенциометрическом определении пропранолола. Природа пластификатора влияет на распределение МИП частиц в поливинилхлоридной пленке, наклон электродной функции, линейный диапазон и коэффициенты селективности пропранолол-селективных сенсоров. Предложенные сенсоры апробированы для определения пропранолола методом прямой потенциометрии в модельных растворах и таблетках фармацевтического препарата.

Ключевые слова: пластификатор; полимер с молекулярными отпечатками; молекулярно-импринтированный полимер; пропранолол; потенциометрический сенсор; сенсор на основе МИП; МИП микросферы.

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ВПЛИВ ПЛАСТИФІКАТОРА НА ХАРАКТЕРИСТИКИ ПОТЕНЦІОМЕТРИЧНОГО СЕНСОРА НА ОСНОВІ ПОЛІМЕРУ З МОЛЕКУЛЯРНИМИ ВІДБИТКАМИ ОБЕРНЕНОГО ДО ПРОПРАНОЛОЛУ

Вперше досліджено вплив різних пластифікаторів на відгук потенціометричних сенсорів на основі полімерів з молекулярними відбитками пропранололу в змішаних неводних середовищах і на коефіцієнт селективності розроблених сенсорів. Пластифікатори (ді-N-октілфталат (ДОФ), дібутилфталат (ДБФ) і діоктілсебацинат (ДОС)) були використані в

сенсорах на основі молекулярно-імпринтованих полімерів (МІП) для зміни властивостей полівінілхлоридної мембрани, поліпшення межі виявлення та селективності електродів при потенціометричному визначенні пропранололу. Природа пластифікатора впливає на розподіл МІП часток в полівінілхлоридній плівці, нахил електродної функції, лінійний діапазон і коефіцієнти селективності пропранолол-селективних сенсорів. Запропоновані сенсори апробовані для визначення пропранололу методом прямої потенціометрії в модельних розчинах і таблетках фармацевтичного препарату.

Ключові слова: пластифікатор; полімер з молекулярними відбитками; молекулярно-імпринтований полімер; пропранолол; потенціометричний сенсор; сенсор на основі МІП; МІП мікросфери.

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Надійшла до редколегії 26.04.13