ELECTROANALYTICAL PERFORMANCE OF ION-SELECTIVE ELECTRODES BASED ON DODECATUNGSTOPHOSPHATE IONOPHORES FOR PHARMACEUTICAL QUANTIFICATION

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Abstract

This study demonstrates a highly sensitive, rapid potentiometric method and advanced ion-selective electrodes (ISEs) utilizing heteropolymetallophosphate ionophores for the determination of target pharmaceuticals. The primary advantages of the proposed sensors include rapid response times, a broad analytical range, and low detection thresholds. The developed membranes exhibit a detection limit of 10^{-5} mol/L and a linear response range extending from 1×10^{-1} to 1×10^{-5} mol/L.

Keywords: Ion-selective electrode, pharmaceuticals, diprazine, bromhexine, ionophore, dodecatungstophosphoric acid.

ЭЛЕКТРОАНАЛИТИЧЕСКИЕ ХАРАКТЕРИСТИКИ ИОНОСЕЛЕКТИВНЫХ ЭЛЕКТРОДОВ НА ОСНОВЕ ДОДЕКАТУНГСТОФОСФАТНЫХ ИОНОФОРОВ ДЛЯ КОЛИЧЕСТВЕННОГО ОПРЕДЕЛЕНИЯ ЛЕКАРСТВЕННЫХ ПРЕПАРАТОВ

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Аннотация

В настоящем исследовании представлен высокочувствительный и быстрый потенциометрический метод, а также усовершенствованные ионоселективные электроды (ИСЭ), использующие в качестве ионофоров гетерополиметаллофосфаты, для определения целевых лекарственных препаратов. Основными преимуществами предложенных сенсоров являются быстрое время отклика, широкий аналитический диапазон и низкие пределы обнаружения. Разработанные мембраны характеризуются пределом обнаружения (10^{-5}) моль/л и линейным диапазоном отклика от (1 \times 10^{-1}) до (1 \times 10^{-5}) моль/л.

Ключевые слова: ионоселективный электрод, лекарственные препараты, дипразин, бромгексин, ионофор, додекатунгстофосфорная кислота.

Farmatsevtik preparatlarni miqdoriy aniqlash uchun dodekatungstofosfat ionoforlari asosidagi ion-selektiv elektrodlarning elektroanalitik ko‘rsatkichlari

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Annotatsiya

Ushbu tadqiqotda muayyan farmatsevtik preparatlarni aniqlash uchun geteropolimetallofosfat ionoforlardan foydalanishga asoslangan yuqori sezgir va tezkor potensiometrik usul hamda takomillashtirilgan ion-selektiv elektrodlar (ISE) taqdim etilgan. Taklif etilayotgan sensorlarning asosiy afzalliklari tezkor javob berish vaqti, keng analitik diapazon va aniqlash chegarasining pastligidan iborat. Ishlab chiqilgan membranalar (10^{-5}) mol/l aniqlash chegarasi hamda (1 \times 10^{-1}) dan (1 \times 10^{-5}) mol/l gacha bo‘lgan chiziqli javob diapazoni bilan tavsiflanadi.

Kalit so‘zlar: ion-selektiv elektrod, farmatsevtik preparatlar, diprazin, bromgeksin, ionofor, dodekatungstofosfat kislota.

Introduction

The rapid expansion of the chemical-pharmaceutical sector coupled with the widespread growth of pharmacy networks globally highlights an increasing demand for rapid, precise, and straightforward analytical methodologies for drug quantification. Solid-contact or liquid-contact plasticized membrane ion-selective electrodes offer a viable and efficient solution to these analytical challenges. Consequently, engineering a new generation of electrochemically active materials and developing high-selectivity sensors based on them represents a crucial objective in modern pharmaceutical analysis.

Literature Review

The objective of this research is to investigate the analytical utility of novel ionophore-based ion-selective electrodes synthesized from dodecatungstophosphoric acid (DTP) and respective drug substrates for the quantitative determination of diprazine (diprazine) and bromhexine in pharmaceutical formulations.

Research Methodology

The ion-selective membranes were fabricated by dissolving a mixture containing polyvinyl chloride (PVC), dioctyl phthalate (DOP) plasticizer, and the electrochemically active complexes—either $Dipraz_3[P(W12O40)]$ —in tetrahydrofuran (THF). To construct the liquid-contact plasticized membrane electrodes, polymeric discs (10 mm diameter) matching the dimensions of the PVC tube were precisely mounted onto the polished terminal ends of the tubes using a specialized adhesive agent.

The electrochemical performance of the fabricated sensors was evaluated by measuring the electromotive force (EMF) of the following galvanic cell configuration:

Ag, AgCl\text{KCl (sat.)\sample solution\membrane\ Internal solution\AgCl, Ag

Prior to potentiometric measurements to evaluate the dependence of the electrode potential on analyte concentration, the ISEs were conditioned in a 1×10^{-3} M solution of the respective drugs. This conditioning phase ensures that the membrane

surface reaches ion-exchange equilibrium with the target analyte ions. All experimental procedures were performed using plasticized membrane electrodes incorporating either Dipraz3[P(W12O40)]or Bromgek3[P(W12O40)] activ

Analysis and Results

To evaluate the potentiometric response functions of the developed ISEs, standard aqueous solutions of diprazine and bromhexine hydrochloride were prepared within a concentration range of 1×10^{-1} to 1×10^{-7} M. For robust statistical validation, six identical electrodes were fabricated and evaluated for each membrane composition.

Figure 1 illustrates the potentiometric calibration curves (Nernstian response regions) of the DTP-based electrodes during the quantification of diprazine and bromhexine hydrochloride.

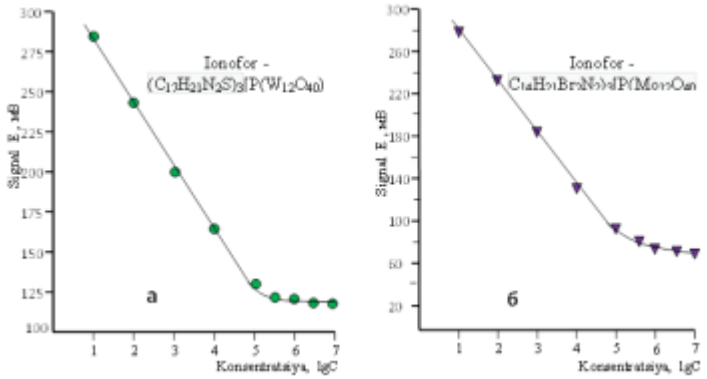


Figure 1. Potentiometric response intervals (Nernstian regions) of ISEs based on heteropolymetallophosphate ionophores: **a)** diprazine hydrochloride; **b)** bromhexine hydrochloride.

As demonstrated in Figure 1, the linear response region of the DTP-functionalized electrodes corresponds to analyte concentrations ranging from 1×10^{-1} to 1×10^{-5} M. This confirms that the investigated complexes remain dissociated within the membrane matrix. Furthermore, the specific nature of the organic cation incorporated into the ionophore structure does not significantly disrupt the fundamental electrochemical attributes of the host membranes.

One of the definitive parameters assessing the quality of any ISE is the slope of its response function. A theoretical Nernstian slope indicates a single-charge ion-transfer process. The developed sensors exhibit both cationic (associated with the drug species) and anionic (associated with the DTP framework) functionalities.

The empirical slope (K) of the ion-selective electrode function (E-pC) can be calculated utilizing the following relation:

K=A/B (1)

where Δ E and Δ pC represent the coordinate variations extracted directly from the linear segment of the calibration graph.

Thus, the electrode slope defines the ultimate sensitivity of the sensor and theoretically matches the pre-exponential factor in the Nernst equation (0.059/z V at room temperature). This value ideally reaches 59 mV/decade for monovalent ions and 29.5 mV/decade for divalent ions. In practice, the relative near-Nernstian behavior (Q%) for a monovalent ion is calculated as follows:

Q%= (K/58)·100

This percentage validates whether the fabricated sensor functions adequately within expected operational limits. The calculated parameters for the response functions of the dodecatungstate-based ISEs in evaluating diprazine and bromhexine are compiled in Table 4.4.

Table 4.4.

Potentiometric response parameters and slope coefficients of ISEs based on dodecamolybdate and dodecatungstate complexes

№	**Ionophore Composition**	**Target Analyte**	ΔE	ΔpC	K	K%
3	C17H21N2S)3[P(W12O40)]	Diprazinee	241	4,53	53,10	90,1
4	(C14H21Br2N2)3[P(Mo12O40)]	Bromgeksin	233	4,12	56,70	96,1

The experimental data detailed in Table 4.4 indicate that the empirical slopes of the developed electrodes correspond to 90–96% of the theoretical Nernstian value. This close agreement firmly establishes the viability of these sensors for routine pharmaceutical analysis.The lower limit of detection (Cmin, p) signifies the

minimum concentration at which the linear correlation between the EMF and analyte activity begins to deviate. To determine (Cmin, p), the linear segments of the E - p*A* response curve are extrapolated. The coordinates of the intersection point yield the -log (Cmin, p) value on the abscissa.

To extract the specific detection limits (Cmin, p) for the DTP-ionophore sensors, potentiometric data were compiled across concentration profiles spanning 10^{-1} to 10^{-7} mol/L for both diprazine and bromhexine hydrochlorides. Figure 2 demonstrates the graphical determination of the lower concentration thresholds utilizing the bromhexine-selective system.

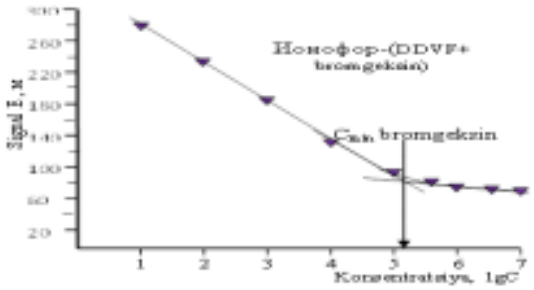


Figure 2. Graphical extraction of the lower limit of detection (Cmin, p) for bromhexine hydrochloride in aqueous media utilizing the DTP-based plasticized membrane electrode.

As illustrated by the plot, the lower limit of detection achieved by the bromhexine-selective electrode corresponds to log (Cmin, p)=-5.1. Below this critical concentration, the potential response flattens out, departing from the Nernstian profile. A uniform characteristics observed across all developed sensors is that at concentrations of 10^{-6} mol/L and below, the potential signal becomes independent of concentration changes. Consequently, these DTP-based membrane configurations are restricted from quantifying these target drugs below a threshold of 10^{-6} mol/L under the specified experimental conditions.

Conclusions

This segment of the work elucidates the interaction regularities between tungsten-containing heteropolymetallophosphate complexes and pharmaceutical agents, culminating in the development of novel ion-selective sensors. The synthesized

heteropolymetallophosphate ionophores were successfully utilized to engineer functional ISEs tailored for monitoring widely used clinical agents, specifically diprazine and bromhexine. The sensitivity and dynamic linear ranges of the sensors were thoroughly validated across a concentration domain of 10^{-1} to 10^{-7} mol/L.

The experimental findings confirm that the highest sensitivity and potentiometric selectivity are attained by the diprazine- and bromhexine-targeted electrode systems. Extrapolation methods revealed that the lower detection limit for the bromhexine-selective sensor reaches log (Cmin, p)=-5.1. Finally, the empirical data were processed via regression analysis, which facilitated the design of rapid analytical protocols suitable for the express determination of dibazole, trimecaine, diprazine, and bromhexine pharmaceuticals.

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