



Development of a Phthalocyanine-Based PVC Membrane Potentiometric Sensor for the Determination of Imipramine

Muge KARADAS AKSAR¹ Gulsah SAYDAN KANBEROGLU^{2*} Mehmet Salih AĞIRTAŞ²

¹Department of Chemistry, Graduate School of Natural and Applied Sciences, Yuzuncu Yil University, Van, Türkiye.

²Department of Chemistry, Faculty of Science, Yuzuncu Yil University, Van, Türkiye.

Received: 21 January 2026; Revised: 7 March 2026; Accepted: 1 April 2026

*Corresponding author : gskanberoglu@yyu.edu.tr

Citation: Karadas Aksar, M., Saydan Kanberoglu, G., & Ağırtaş, M.S. (2026). Development of a phthalocyanine-based PVC membrane potentiometric sensor for the determination of imipramine. *International Journal of Chemistry and Technology*, 10, 1-10. <http://dx.doi.org/10.32571/ijct.1868961>

ABSTRACT

Imipramine is a tricyclic antidepressant. Overdose of imipramine may cause gastrointestinal upset, dizziness, blurred vision, increased appetite, drowsiness, constipation, dry mouth, urinary retention, narrow-angle glaucoma, and delirium. It can cause life-threatening side effects, particularly severe hypotension, coma, hyperactive reflexes, cardiac dysrhythmias, convulsions, and hypothermia confusion. Therefore, the development of a sensitive, reliable, low-cost, and simple method such as potentiometry for the determination of IMIP (imipramine) is of great importance. In this study, a phthalocyanine derivative, [2,10,16,24-tetrakis{9,9-bis(4-oxyphenylfluorene)phthalonitrile}phthalocyanine cobalt(II) (BS-Co-1)], was used as the ionophore in the structure of the imipramine-selective sensor developed. The sensor demonstrated high selectivity towards imipramine, wide linear working range (5.0×10^{-8} to 1.0×10^{-2} mol L⁻¹), wide pH working range (2.18-7.38), short response time (20 seconds), and high repeatability. Furthermore, the analytical application of the sensor has been carried out in a commercial drug. The sensor performed well with a recovery of 98.4%.

Keywords: Imipramine, phthalocyanine, potentiometric sensor, ionophore.

1. INTRODUCTION

As a tricyclic antidepressant, imipramine is used to treat bulimia, attention deficit disorder, and depression. It is also used as an adjunct in the treatment of nocturnal enuresis in children aged six and older (Hearn et al., 2014; Caldwell et al., 2016; Giwa and Oey, 2018; Dean and Kane, 2025). Overdose with imipramine can cause

gastrointestinal discomfort, dizziness, blurred vision, increased appetite, drowsiness, constipation, dry mouth, urinary retention, narrow-angle glaucoma, and delirium. It can cause life-threatening side effects, particularly severe hypotension, coma, hyperactive reflexes, cardiac dysrhythmias, convulsions, and hypothermia confusion. It has been reported that imipramine use may increase suicidal thoughts in individuals under the age of 24,

especially early in treatment. On the other hand, it can also trigger manic or mixed episodes in individuals with bipolar disorder. Therefore, imipramine determination is crucial (Food and Drug Administration, 2004; Ünverir, 2007; Khakpai et al., 2021; Zengin and Sabak, 2023; Jafari et al., 2024).

Many analytical methods have been used in the literature for the determination of imipramine. These methods include voltammetry (Sanghavi and Srivastava, 2013; Yamuna et al., 2021; Karikalan et al., 2022), reversed-phase chromatography with ultraviolet and coulometric detectors (Foglia et al., 1991), spectrophotometry (El Zeany et al., 2003; Azmi et al., 2022), high-performance liquid chromatography (HPLC) (Rezazadeh and Emami, 2016; Zhao et al., 2016; Pradeep Nalawade et al., 2025), electrochemiluminescence (Yu et al., 2011), chemometry (Markopoulou et al., 2005; Riahi et al., 2009) and gas chromatography (GC) (Pommier et al., 1997). Many of the methods mentioned are time-consuming and require environmentally hazardous solvents, laborious pretreatment steps, complex instrumentation, specialized operators, and expensive consumables (Chew et al., 2021; Parys et al., 2022; Talath and Hani, 2024). The identification of substances affecting human health, such as pharmaceuticals and their metabolites, environmental pollutants, and food additives, is of paramount importance today. Therefore, there is a great deal of interest in reliable, rapid, sensitive, and accurate analytical methods. Electrochemical methods stand out due to their low-cost instrumentation, high sensitivity, stability, environmental friendliness, and on-site monitoring capabilities (Elsayed, 2023; Crapnell et al., 2024; Pimpilova, 2024).

Potentiometric sensors, which are electrochemical sensors, stand out as an alternative to many of the detection methods mentioned above for the determination of imipramine, due to their remarkable features such as wide linear range (LR), high selectivity, low detection limit, non-damage to the measured sample, no pretreatment required, and the ability to detect even in colored and sedimentary solutions (Özbek et al., 2020; Yalcin et al., 2023; Fathy and Bühlmann, 2025). Potentiometric sensors are commonly used to analyze ion concentrations in clinical, environmental, and food samples. They are relatively inexpensive to implement and offer rapid and easy measurements. Currently, the most commonly used model in potentiometric analysis is the solid-contact ion-selective electrode (Wardak et al., 2023; Gao et al., 2024; Ali et al., 2025).

The key component in the selectivity of ion-selective electrodes is ionophores, called lipophilic complexants, which selectively bind the analyte and complex weakly with other ions and strongly with the analyte ions. As the most important components of the selective

membrane, ionophores are mobile molecules that bind to ions and facilitate their transport across the membrane (Johnson and Bachas, 2003; Bondar et al., 2022; Gao et al., 2024). The ion-active groups to which the ions bind are large and hydrophobic. Because the ion-active groups in the ionophore are polar, they bind ions at the interface formed by the organic excess water, while the hydrophobic portions allow the ionophore to adhere to the organic phase. Ionophores are responsible for the membrane's selectivity. They should be more selective for the target analyte than for interfering or secondary ions. It can be thought that the reason why an ion-selective electrode shows different selectivity towards ions other than the analyte is that the interaction between the ionophore used in the electrode and the analyte is different from its interaction with other ions (Shamsipur et al., 2001; Bondar et al., 2022; Zhai et al., 2022).

The use of phthalocyanines as ionophore has recently attracted particular attention. Phthalocyanines (Pc) are aromatic macrocyclic compounds with a sharp blue-green color, a relatively stable two-dimensional 18- π -electron conjugated system. The binding of various elements to the central coordination domain of the macrocycle and the addition of various functional substituents in peripheral and non-peripheral positions to the aromatic moiety confer electrochemical, catalytic, photoconductive, photovoltaic, light absorption, electrical conductivity, and photoexcitability properties to phthalocyanines. They are particularly useful as ionophores in potentiometric sensors (İpek et al., 2017; Escayola et al., 2024; Jebali et al., 2025; Turan and Koca, 2025). In addition to these superior properties, phthalocyanines have another important characteristic: a wide range of operating potential in both anodic and cathodic states. This is because they are easily reduced and oxidized. This ability to operate within these wide potentials allows the sensor to have a wide pH working range. In particular, when metallophthalocyanines are used in the preparation of sensors, they increase the selectivity of the sensor. This enables analysis of complex samples (Valli, 2005; Demir et al., 2022).

Metal organic framework (MOF) (MIL-53(Al)) (Subasi et al., 2022) and ion pair (imipramine-tetraphenyl borate) (Javanbakht et al., 2009) have been used as ionophore for the determination of imipramine previously in the literature. However, to the best of our knowledge, phthalocyanine has not been used as an ionophore for the determination of imipramine so far. In this study, phthalocyanine was used as an ionophore for the first time in the development of a potentiometric sensor for imipramine determination. From this perspective, the study represents a significant advancement compared to previously developed potentiometric sensors, exhibiting a very low detection limit ($2.0 \times 10^{-8} \text{ mol l}^{-1}$) and a wide linear range (5.0×10^{-8} - $1.0 \times 10^{-2} \text{ mol l}^{-1}$).

2. MATERIALS and METHODS

2.1. Chemicals, Devices and Apparatus Used in the Experiment

Imipramine hydrochloride ($\geq 99\%$, USA) was purchased from Sigma-Aldrich. Dibutyl phthalate (DBP), Antimony(III) chloride, bis(2-ethylhexyl) sebacate (DOS), tetrahydrofuran (THF), glucose, NPOE (nitrophenyl octyl ether), and PVC, were purchased from Sigma-Aldrich (Germany). Barium nitrate and copper (II) nitrate trihydrate were purchased from ZAG chemical (Turkey). Cadmium nitrate tetrahydrate and orthophosphoric acid (85%) was purchased from the company CARLO ERBA (France). Iron(II) nitrate hexahydrate (Turkey) was purchased from Tunaplastik company. Iron(III) nitrate nonahydrate (USA) was purchased from Bostonchem. Lithium nitrate (United Kingdom), and cerium(III) nitrate hexahydrate (Germany) were purchased from Sigma-Aldrich; Nickel(II) nitrate hexahydrate (United Kingdom), magnesium nitrate hexahydrate (Germany), potassium nitrate (Germany), cobalt(II) nitrate hexahydrate (Germany), ammonium nitrate (Germany), sodium hydroxide (Germany), cobalt (II) nitrate hexahydrate (Germany) and sodium nitrate (Germany) were purchased from Merck; and aluminum nitrate nonahydrate (Germany) was purchased from ROTH. All of these materials were used with analytical grade. In this study, Desmodur RFE (hardener, Bayer, Germany) and TP3100 (epoxy, Denlaks, Turkey) were used for the preparation of the solid contact. For analytical application, pharmaceutical preparation (tofranal) were procured from local pharmacy in Turkey. The potentiometric measurements were conducted using a high-input-impedance home-made multi-channel potentiometer in combination with a silver/silver chloride reference electrode (Gamry, USA). A NeoMet pH meter was used for pH measurement. A WiseMix vortex was used to mix the membrane. Weighing was done with a RADWAG precision balance.

2.2. The Process of Preparing Sensors for Imipramine Determination

As reported in the literature, the sensor preparation process consists of two steps (Kanberoglu and Kaya, 2026). The first step is the preparation of the solid contact, and the second step is the preparation of the membrane compositions. In potentiometric sensors, solid contacts enable ion-electron conversion within the sensor and increase its stability (Kamel et al., 2020; Shao et al., 2020). To prepare the solid contact, 50% graphite, 35% epoxy, and 15% hardener are first added to a watch glass. Then, using THF as a solvent, it is mixed until a homogeneous mixture is obtained. Once the appropriate viscosity was achieved, the exposed surface of a copper wire (approximately 0.4-0.5 mm in diameter and 10-15 cm in length) was coated by dipping

it into this mixture 4-5 times. The electrode, coated with a solid contact, is kept in a dark environment for 24 h. PVC membrane compositions are prepared by dissolving a mixture containing a fixed type and ratio of ionophore (3 mg) and PVC (32 mg), different types and ratios of plasticizers (DBP, DOS and NPOE) and in some cases 1 mg KTpClPB in THF solvent. The solid contact surfaces are coated by dipping them 4-5 times into the PVC membrane cocktail with the composition given above and left to dry in a dark environment at room temperature for 24 h. Then, the electrodes are left to condition in a 1.0×10^{-2} M imipramine HCl solution for 12 hours. Thus, the electrodes are ready for measurement. The sensors were stored in the dark during the preparation phase to prevent potential photochemical changes in the solid contact and membrane components, thus maintaining consistent potentiometric behavior and stability.

2.3. Preparation of Sample Used in the Experiment

For the preparation of sample S1, 10 tablets of the commercial drug called tofranal were taken and ground thoroughly, and the amount corresponding to an average tablet was dissolved in 100 mL of pH 3.1 phosphate buffer. The prepared S1 sample was used directly in potentiometric measurements without any filtration, filtering, or separation process.

3. RESULTS and DISCUSSION

3.1. Determination of an Imipramine-Selective Sensor and Investigation of its Performance Characteristics

To determine the best sensor for imipramine determination, different membrane compositions were prepared using BS-Co-1 as the ionophore. Then, the performance characteristics (detection limit (LOD), linear working range (LR), slope, and R^2) of the sensors prepared with these membrane compositions were investigated. When determining the best membrane composition, parameters such as a low detection limit, a wide linear range, a slope value conforming to the Nernst equation, and an R^2 value close to 1 were considered (Table 1). Measurements were performed using 1.0×10^{-8} - 1.0×10^{-2} mol L^{-1} imipramine HCl solutions (phosphate buffer (pH 3.1)). The type and ratio of components (ionophore, plasticizer, polymer, and ionizer) used to prepare the membrane greatly affect the sensor's performance. Thus, determining the ideal membrane composition for potentiometric sensors is important. Table 1 shows that sensor number 3 has better performance characteristics compared to the other sensors. Therefore, sensor number 3 was determined as an imipramine-selective sensor. The membrane composition used to prepare this sensor consists of PVC (32 mg), BS-Co-1 (3 mg), DBP (64 mg), and KTpClPB (1 mg). The instantaneous potential values obtained using the imipramine-selective sensor in the mentioned

concentration range (1.0×10^{-8} – 1.0×10^{-2} mol l⁻¹) and the calibration graph obtained using the potential values read against the studied log[IMIP] values are shown in Figure 1. The sensor showed a linear response to imipramine ($R^2 = 0.9989$) with a slope value of 59.6 in the concentration range of 1.0×10^{-2} – 5.0×10^{-8} mol l⁻¹. The detection limit (LOD) of the proposed potentiometric sensor is typically determined by the intersection point of the extrapolated linear portions of the calibration curve, specifically the high-concentration Nernstian region and the low-concentration non-Nernstian or baseline region (Buck and Lindner, 1994; Fernández-Ramos et al., 2011). LOD of the imipramine-selective sensor was determined as 2.0×10^{-8} mol l⁻¹. High selectivity of phthalocyanine-based sensors towards organic cations has been previously reported in the literature (Kaya et al., 2025; Kanberoglu et al., 2026). The sensor behaves selectively towards imipramine due to synergistic interactions between the cationic imipramine species (IMIP⁺) and the cobalt phthalocyanine ionophore. Electrostatic attraction between the electron-rich phthalocyanine macroring and the protonated tertiary amine of imipramine, along with π – π stacking between the extended π -system of phthalocyanine and the aromatic rings of imipramine, stabilizes the ion-ionophore complex within the hydrophobic PVC membrane phase. Thus, the hydrophobic substituents of phthalocyanine promote the migration of imipramine into the membrane phase, enhancing the potentiometric response. The solid-contact structure of the sensor facilitates ion transfer, strengthening the phthalocyanine–IMIP⁺ interaction and increasing sensor stability (Hassan et al., 2005; Kamel et al., 2020; Shao et al., 2020; Ciucu et al., 2025; Yavuz, 2025).

3.2. Investigation of Sensor Repeatability and Response Time

Repeatability is crucial for a sensor. Low repeatability indicates that the sensor is unreliable. To determine the reliability of the sensor, sequential measurements were performed in imipramine HCl solutions prepared at different concentrations (1.0×10^{-7} , 1.0×10^{-6} and 1.0×10^{-5} mol l⁻¹). The aim was to see if the sensor gave similar

potential responses at the same concentrations. By calculating the sensor's mean and standard deviation from these potential values, we can gain insight into the sensor's repeatability using these statistical data. The mean and standard deviation values obtained for 1.0×10^{-7} , 1.0×10^{-6} and 1.0×10^{-5} mol l⁻¹ imipramine HCl solutions were determined as 2635.6 ± 0.9 , 2689.6 ± 0.5 and 2745.0 ± 0.7 , respectively. As can be seen from these results, the standard deviation values are quite low even at low concentrations, demonstrating the high repeatability of the sensor (Figure 2a).

Another important parameter for potentiometric sensors is the response time (RT). The short response time of these sensors distinguishes them from other existing analytical methods (HPLC, liquid chromatography–mass spectrometry, and GC) and makes them advantageous. The response time of the developed sensor was evaluated in standard imipramine HCl solutions (Figure 2b). According to IUPAC, response time is 95% of the time it takes for the potential to stabilize, and is denoted as t_{95} (Bakker and Pretsch, 2005; Mohan and Kumar, 2021; Gao et al., 2024). The imipramine-selective sensor was determined to have a short response time of 20 seconds (Figure 2b).

3.3. The Effect of pH on the Imipramine-Selective Sensor

To ensure the sensor provides accurate analysis results, it is crucial to determine the pH range it is unaffected by. The effect of pH on the sensor's response was evaluated in 10^{-4} mol l⁻¹ and 10^{-5} mol l⁻¹ imipramine HCl solutions. During the measurements, 1 mol l⁻¹ HCl was used as the acid and 1 mol l⁻¹ NaOH as the base. The acid and base were added gradually to the prepared imipramine HCl solutions. Potentials were measured in response to varying pH values and plotted on a graph. It was determined that the pH range unaffected by the sensor was 2.18–7.38 (Figure 3). However, a decrease in potential occurred when the pH rose above 7.38. This situation can be attributed to the increasing amount of OH⁻ ions and the decreasing amount of protonated imipramine.

Table 1. Sensors and performance characteristics prepared using BS-Co-1 as an ionophore.

Sensor no	Sensor composition, w/w % (mg)						LR (mol l ⁻¹)	Slope (mV/decade)	R ²	LOD (mol l ⁻¹)
	Ionophore (BS-Co-1)	PVC	NPOE	DBP	DOS	KTpCIPB				
1	3.0	32.0	64.0	-	-	1.0	1.0×10^{-6} – 1.0×10^{-2}	47.1	0.9826	1.0×10^{-6}
2	3.0	32.0	65.0	-	-	-	1.0×10^{-5} – 1.0×10^{-2}	60.9	0.9976	1.0×10^{-5}
3	3.0	32.0	-	64.0	-	1.0	5.0×10^{-8} – 1.0×10^{-2}	59.6	0.9989	2.0×10^{-8}
4	3.0	32.0	-	65.0	-	-	1.0×10^{-6} – 1.0×10^{-2}	60.3	0.9864	1.0×10^{-6}
5	3.0	32.0	-	-	64.0	1.0	1.0×10^{-5} – 1.0×10^{-2}	68.1	0.9981	1.0×10^{-5}
6	3.0	32.0	-	-	65.0	-	1.0×10^{-5} – 1.0×10^{-2}	54.9	0.9799	1.0×10^{-5}

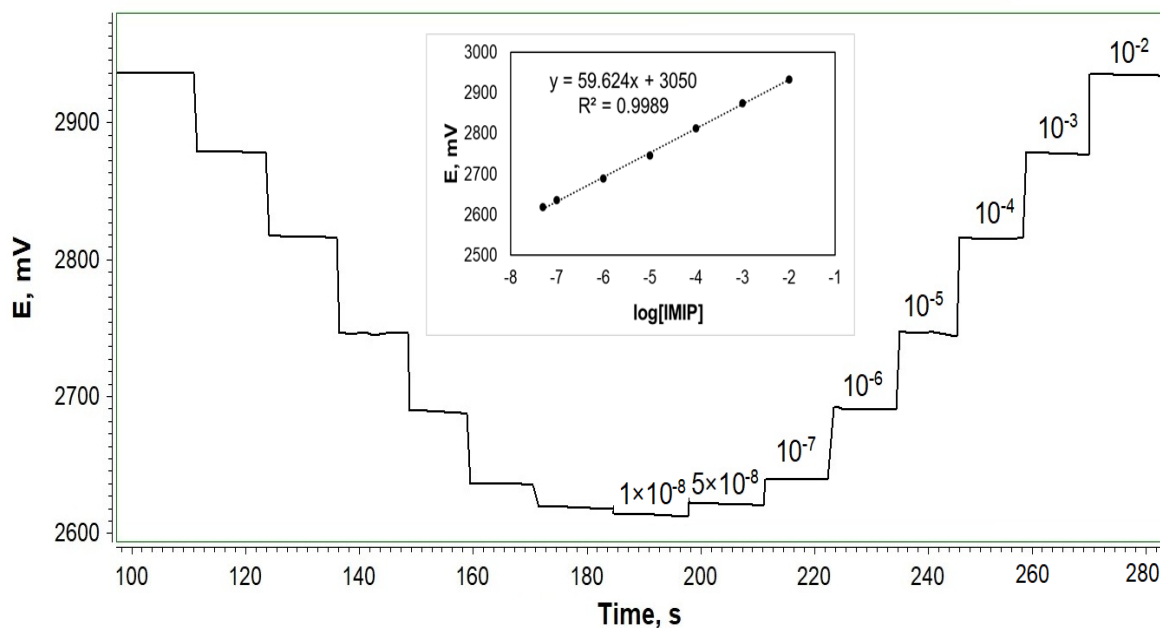


Figure 1. Response of the imipramine selective sensor in imipramine HCl solutions (1.0×10^{-2} - 1.0×10^{-8} M) and its calibration curve.

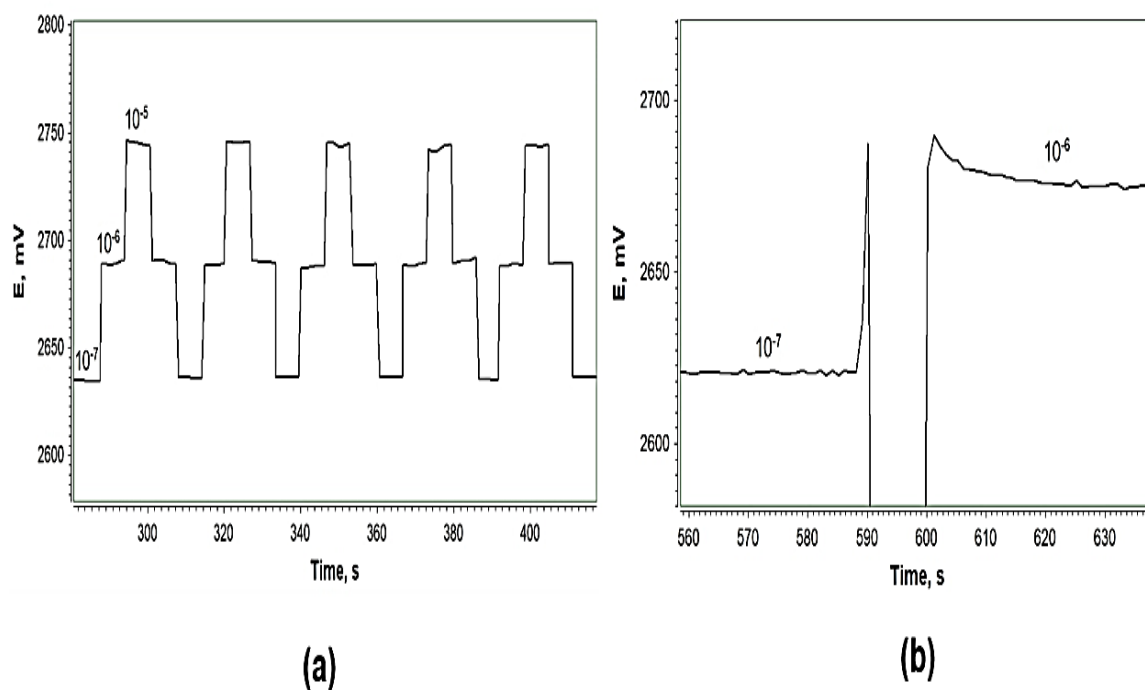


Figure 2. (a) A graph showing the repeatability of the developed sensor. **(b)** An example graph showing the response time of the developed sensor.

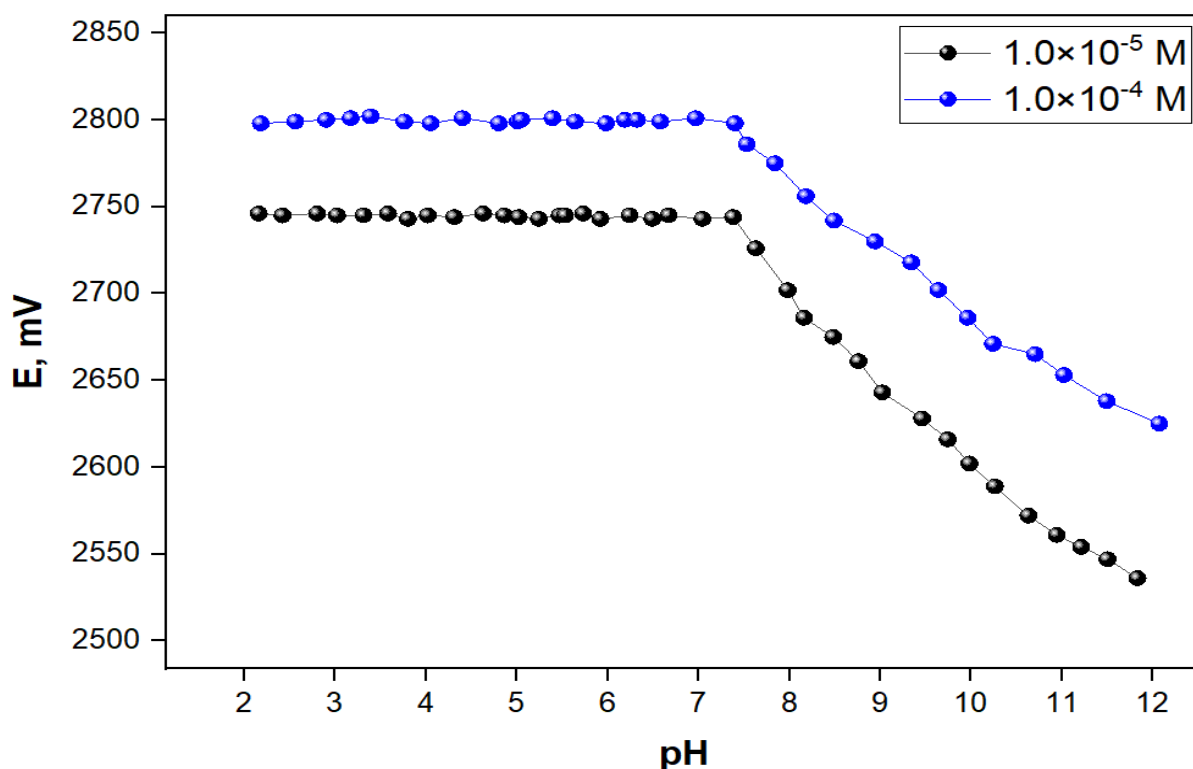


Figure 3. pH working range of the imipramine-selective sensor.

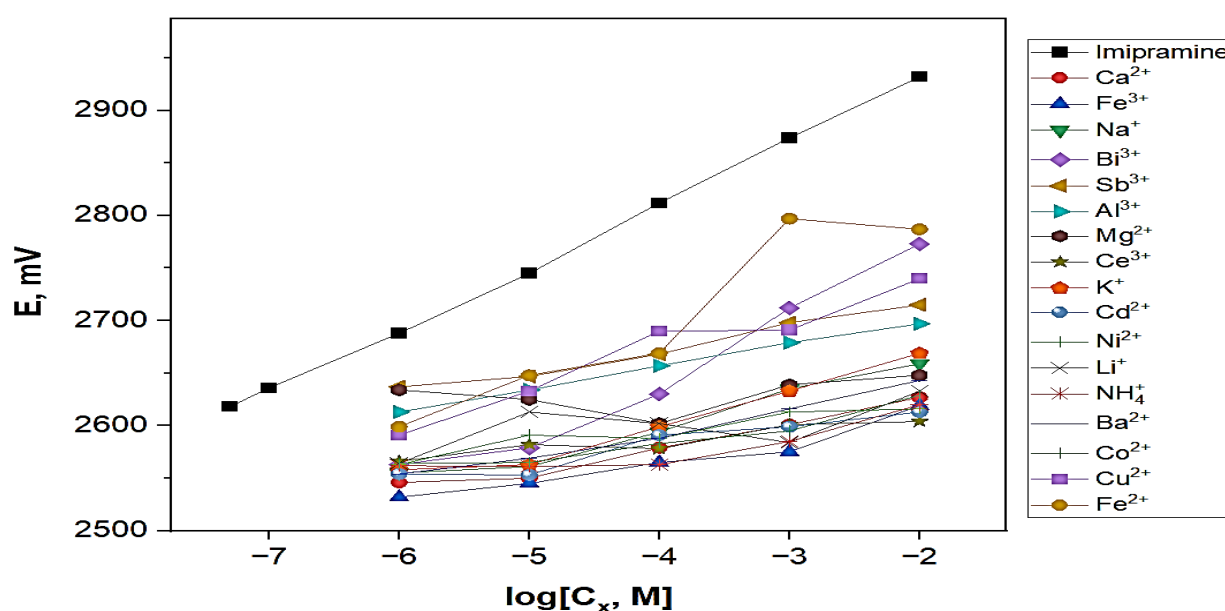


Figure 4. Selectivity graph of the imipramine-selective sensor.

3.4. Selectivity of the Imipramine-Selective Sensor

Selectivity is one of the most critical performance parameters determining the analytical value of a potentiometric sensor. Selectivity refers to the extent to which the sensor's unique response to the target (primary) ion is preserved in the presence of other

(disruptive) species. While an ideal sensor would only respond to the target ion, in reality, other ions with similar physical or chemical properties can also affect the sensor potential. The interference effect of 17 different species on the potentiometric response of an imipramine-selective sensor was investigated (Bakker et al., 2000; Mohan and Kumar, 2021).

Selectivity coefficients (Table 2) were calculated based on measurements made using the separate solution method (Formula 1) (Umezawa et al., 2000).

$$\log K_{A,B}^{pot} = \frac{(E_B - E_A)Z_A F}{RT \ln 10} + \left(1 - \frac{Z_A}{Z_B}\right) \log a_A \quad (1)$$

The resulting selectivity graph is presented in Figure 4. Considering the results, the substance with the highest interference effect is Fe^{2+} , and even in the presence of this substance, the selectivity of the sensor against imipramine is at least 1000 times.

Table 2. Selectivity coefficients obtained for commonly occurring ions.

Species	K	-logK
Ca^{2+}	8.13×10^{-7}	6.09
Fe^{3+}	2.74×10^{-7}	6.56
Na^+	2.75×10^{-5}	4.56
Bi^{3+}	1.06×10^{-4}	3.97
Sb^{3+}	1.12×10^{-5}	4.95
Al^{3+}	5.59×10^{-6}	5.25
Mg^{2+}	1.82×10^{-6}	5.74
Ce^{3+}	1.54×10^{-7}	6.81
K^+	4.07×10^{-5}	4.39
Cd^{2+}	4.68×10^{-7}	6.33
Ni^{2+}	5.25×10^{-7}	6.28
Li^+	1.02×10^{-5}	4.99
NH_4^+	6.16×10^{-6}	5.21
Ba^{2+}	1.48×10^{-6}	5.83
Co^{2+}	8.71×10^{-7}	6.06
Cu^{2+}	6.46×10^{-5}	4.19
Fe^{2+}	3.89×10^{-4}	3.41

3.5.Examining the Performance Stability of the Developed Sensor Through Daily Measurements

Daily measurements were taken in standard imipramine hydrochloride solutions to evaluate how the performance of the developed sensor changed over time. The daily slope values obtained from the measurements were plotted against time (Figure 5). Analysis of the data shows no significant change in the slope values during the first 32 days. However, a significant decrease in the slopes was observed after the 32th day. These findings indicate that the developed sensor has an effective lifetime of 32 days after preparation and its performance remains largely unchanged.

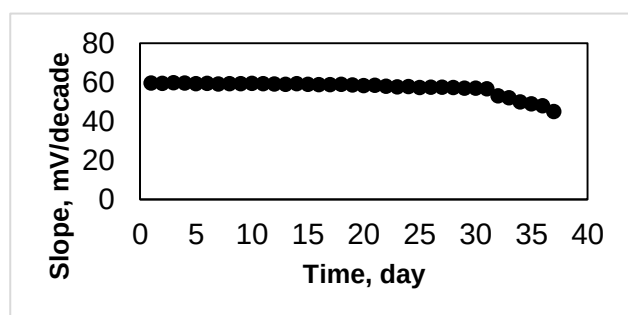


Figure 5. Graph showing the lifetime of the imipramine-selective sensor.

3.6.Analytical Application of the Sensor and Comparison with Potentiometric Sensors Developed in the Literature

The analytical applicability of the sensor was tested on a commercial drug called Tofranil, obtained from a local pharmacy in Turkey. After calibration in standard imipramine HCl solutions prepared in buffer, the potential of sample S1 was measured. The amount of imipramine HCl in sample S1 was determined using the calibration graph. The statistical results for sample S1 are presented in Table 3. The sensor demonstrated high accuracy, achieving a 98.4% recovery rate in the sample. The sensor's recovery value (98.4%) in drug determination was quite good, and it yielded successful results in sample analysis.

Only two different potentiometric sensors have been developed in the literature for the determination of imipramine. Subasi et al. (2022) also used MIL-53(Al), a MOF structure, as the ionophore. Compared to the sensor developed in this study, it achieved a shorter response time and a longer lifetime. However, the sensor developed in this study has a wider linear working range and a lower detection limit. Javanbakht et al. (2009) used the imipramine-tetraphenylborate ion pair as an ionophore in the structure of the sensor they developed and reported a shorter response time than the sensor we developed. Our study has the advantage of a lower detection limit and a wider linear working range, as well as a longer lifetime compared to the sensor developed by Javanbakht et al. (2009) (Table 4).

4. CONCLUSION

Due to their extensive conjugated π -electron system and electron-donating properties, phthalocyanines are selective and sensitive to the target analyte in sensor studies. The macrocyclic structures of phthalocyanines interact with imipramine via hydrogen bonding, coordination, π - π stacking, or van der Waals interactions, forming a reversible complex that allows the sensor to give a selective potentiometric response to imipramine. Furthermore, phthalocyanines exhibit high thermal and chemical stability, extending the sensor's lifetime. In this study, BS-Co-1 was used as the ionophore in the potentiometric sensor developed for imipramine determination. Among sensors prepared with different membrane compositions, sensor number 3 showed the best performance and was therefore determined as the imipramine-selective sensor. The membrane composition used in the preparation of this sensor consists of 32% PVC, 64% DBP, 1% KTpClPB, and 3% BS-Co-1. The developed sensor has a 32-day lifetime, a linear range of 5.0×10^{-8} – 1.0×10^{-2} mol l^{-1} , an LOD value of 2.0×10^{-8} mol l^{-1} , a response time of 20 seconds, and an pH range of 2.18–7.38. The developed sensor exhibits high selectivity for imipramine in the presence of commonly found ions, enabling accurate

measurements even in complex matrices. Furthermore, this study serves as a guide for future research due to the first-ever use of phthalocyanine as an ionophore for imipramine determination and its lower detection limit

and wider linear range compared to previously reported potentiometric sensors. The sensor has been successfully applied in pharmaceutical preparation.

Table 3. Statistical evaluation for sample S1.

Sample	Label value (mg/tablet)	Found value (mg/tablet) (N=5)	Recovery (%)	Er (%)
S1 (Tofranil)	25.0	24.6±0.2	98.4	1.6

Table 4. comparison of the imipramine-selective sensor developed in this study with potentiometric sensors reported in the literature for the determination of imipramine.

Reference	Ionophore	LR (mol l ⁻¹)	LOD (mol l ⁻¹)	Slope (mV/decade of concentration)	RT (s)	Life- time (day)
Subasi et al., 2022	MIL-53(Al)	1.0×10^{-7} - 1.0×10^{-1}	5.0×10^{-8}	57.7	<5	55
Javanbakht et al., 2009	Imipramine-tetraphenyl borate	1.0×10^{-5} - 1.0×10^{-1}	7.0×10^{-7}	55.1	15	28
This work	BS-Co-1	5.0×10^{-8} - 1.0×10^{-2}	2.0×10^{-8}	59.6	20	32

Acknowledgements

We would like to thank Van Yuzuncu Yil University, Scientific Research Projects Coordination Office (Project No = FYL-2025-12317) for their financial support. We would also like to thank Nurcan KAYA for her unwavering support in this study.

Ethical Statement

This research was carried out in compliance with ethical research principles. The authors confirm that all data were collected and reported in accordance with academic integrity rules. There is no conflict of interest, and the manuscript has not been submitted or published elsewhere.

Conflict of Interest

There is no conflict of interest.

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