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Molecularly Imprinted Polymer Based Potentiometric Sensor for the Selective and Sensitive Detection of Nerve Agent Simulant Parathion

Ozan Yağmuroğlu

Chemistry Department, Turkish Air Force Academy, Istanbul, Turkey
E-mail: oyagmurog@hho.msu.edu.tr

ABSTRACT

In this study, a potentiometric sensor was developed for the analysis of the parahtion which is a nerve agent simulant and pesticide. A molecularly imprinted polymer was used as the recognition layer in the electrode used in the potentiometric sensor. Parathion is also used as both an organophosphorus pesticide and a nerve agent simulant. For this reason, analysis methods to be developed for parathion are very important. The most important advantages brought by MIP-based sensor systems are; fast analysis, sensitive analysis, and the ability to analyze at very low concentrations. The sensor developed in our study was validated for parathion adsorption. In our study, first, Parathion imprinted polymers were synthesized. The synthesized MIPs are used as the recognition layer in the potentiometric sensor. The characterization of parathion imprinted polymers was done by FESEM, FT-IR, and zeta-sizer measurements. Optimization of the working conditions was carried out for the developed sensor system. The working pH was found to be 7.4.Measurements were taken for parathion samples with different concentrations under optimum operating conditions. When the results obtained were examined, a large linear range (10^{-8}-10^{-4} mol L^{-1}) and a satisfying detection limit against parathion (1.86×10^{-8} mol L^{-1}) were calculated. Interference effect analysis was carried out within the scope of the performance tests of the potentiometric sensor. The analysis showed that interference did not affect the experimental results. In order to examine the matrix effect of the real sample environment, analyses were carried out in tap water and lake water. The recovery values in the analysis results are quite good. The results of the experiments show that the sensor we have developed can be used successfully in complex matrix environments.

Keywords: Organophosphates; Parathion; Molecularly imprinted polymers; Potentiometric sensor; Chemical warfare agent

1. INTRODUCTION

Chemicals used in chemical weapons and having toxic effects on living things are defined as chemical warfare agents. In the Chemical Weapons Convention, any material used to spread chemical warfare agents is defined as a chemical weapon. Chemical weapons are not only used to kill or injure living things. Chemical weapons can also be used for purposes such as rendering strategically important facilities inoperable, disrupting the enemy's operational plans in a war environment, and creating panic among the people[1]. Different criteria can be considered when classifying chemicals. While determining the criterion, it is important from which point of view the issue is viewed. The classification of chemical warfare agents is based on their physical state, toxicology, and volatility. Chemical warfare agents are evaluated under five classes. These are choking agents, non-lethal chemical agents, blood poisoning agents, nerve agents, blister agents, and blood poisoning agents. The chemicals used to make nerve agents are members of the same family of molecules as the chemicals used to make pesticides. One of the biggest risks in agricultural activities is microorganisms that harm plants. Pesticides are used to protect against the harmful effects of these microorganisms[2-4]. The most commonly used method of pest control in the agricultural field is pesticide use. This is because pesticides give more effective and faster results when used appropriately. In this way, the development of the crop grown in the field is ensured to be in the desired shape. When using pesticides, they are required to be effective only on the pests selected. However, during their use, they can mix with air, water, and soil, and cause harm to living creatures outside the target. In addition, due to unconscious use, they accumulate in high levels in water, soil, vegetable and animal foods[5]. It is possible to group pesticides according to the parasite types they are used to destroy and the chemical components in their structure. Insecticides are pesticides used to destroy insects living in plants, soil, and animals. They are used extensively in Turkey. Herbicides are pesticides used to combat weeds in agriculture[4, 6, 8].

The general molecular structure of nerve agents is included in organophosphorus molecules. Insecticides are also included in this molecule family[4]. Organophosphorus compounds are active in the nervous system in living metabolism. Organophosphates have lipid solubility[9]. These molecules are absorbed into the body through the skin, mucous membranes, eyes, and respiratory system. Organophosphorus molecules generally contain phosphate atoms, oxygen, or sulfur[3,10]. Substituents R1-R2; may be hydrogen, alkyl, aryl, alkoxy or amino groups[2,11]. Substituent X may be a halogen, cyano, or thiol

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group. AChE is a serine hydrolase in terms of its mechanism of action. The AChE enzyme breaks down acetylcholine, which is used in nerve conduction. Organophosphorus molecules prevent the AChE enzyme from performing its function in the body.

Parathion is an organophosphorus insecticide. It was discovered in 1940. Its chemical formula is $C_{10}H_{14}NO_5PS$ (Figure 1). Its molecular mass is 291.3 g/mol. After being absorbed into the body, it interrupts the nerve transmission. Post-exposure symptoms include chills, vomiting, and shortness of breath.

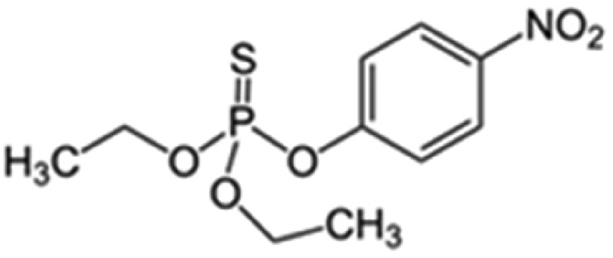


Figure 1. Parathion's molecular structure.

Devices that provide data that can be used in response to a particular measure are generally called sensors. If the signals are obtained as a result of chemical interaction, the sensor is called a chemical sensor[12-14].

Electrochemical sensors have many advantages. Some of those; analyte selectivity, fast analysis and cheapness[15-21]. The methods that analyze samples by measuring potential in electrochemical cells are generally called potentiometric methods.

Potentiometric sensors have many advantages. These include ease of preparation, rapid response, wide working range, device simplicity, and good selectivity[22]. When the literature is examined, it is seen that electrochemical detection-based sensors have been developed for parathion detection. The detection limits of the sensors developed with the electrochemical approach are quite low[23].

In addition, potentiometric sensors using molecularly imprinting technology are very promising[24]. The duration of analysis of potentiometric sensor systems is relatively fast compared to other methods. However, potentiometric sensor studies using MIP in the recognition layer are very rare[25-28].

By the molecular imprinting technique, polymers with the recognition layer of the target molecule are obtained. Cross-linked monomers polymerize around the target molecule. After polymerization, the target molecule is removed. A schematic representation of the processes applied to molecular printed polymer is given in Figure 2. Thus, a template having the same dimensional characteristics as the molecule is obtained in the polymer. The resulting template can bind selectively to the target molecule. Since the molecular imprinting technique achieves the target molecule's specific binding, it can be used in the separation processes. Examples include chromatographic separation, solid phase extraction, and chiral separation. In addition, the MIP technique has been widely used as a recognition layer in chemical sensor systems[29]. Thus, MIP has become an alternative that can be used as an ionophore in potentiometric analysis.

In recent years, many potentiometric sensors have been developed that use MIPs as recognition layers in the analysis of environmental samples. Potentiometric sensors using MIP as a recognition layer have been developed that perform very well in the analysis of chemicals that are harmful to the environment and humans[30-33].

In addition to the analysis of toxic chemicals, MIP-based potentiometric sensors have been developed for the analysis of pharmaceuticals. Sales et al. developed a potentiometric sensor for the analysis of ciprofloxacin. The detection limit of this sensor was calculated as 1.0 x10^{-5} mol/L[34-35].

Similar to the method mentioned above, MIP-based potentiometric sensors have been developed in oxytetracycline and chlorpromazine ions. The detection limit for these

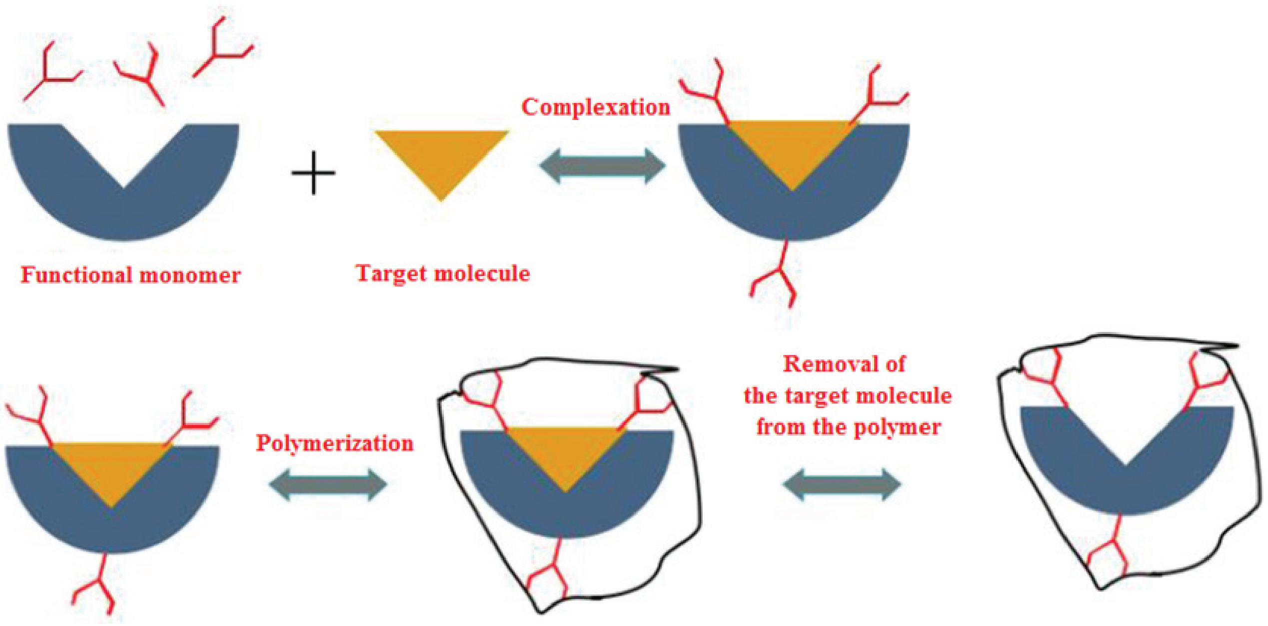


Figure 2. Molecular printed polymer preparation steps.

molecules was found to be 19.8 mg/mL and 0.46 mg/mL, respectively[36-37].

According to Al Azab et al. As a result of his work, he developed a potentiometric sensor for the pesticide dinotefuran. The detection limit of his sensor system was 0.35 mg/L. Agostino et al. developed a potentiometric sensor for atrazine. The detection limit of this sensor was 2.0 x 10^{-5} mol/L[38-40].

In this study, parathion imprinted polymers were synthesized using N-methacryloyl-L-serine monomer (MA-Serine). The polymer synthesized for use in the molecular imprinting technique showed high selectivity and affinity for parathion from a water sample. The serine group, which is a functional group in the polymer, is linked to parathion by electrostatic interaction. In this study, an efficient, low-cost sensor system with easy-to-use, high selectivity to detect parathion was developed.

2. EXPERIMENTAL WORK

2.1 Chemicals

Dibutyl phthalate (DBP), L-Serine, 2,2-azobisisobutyronitrile (AIBN), Methacryloyl benzotriazole (MA-Bt), Ethylene glycol dimethacrylate (EDMA), parathion, NaOH and other chemicals were bought from Sigma-Aldrich Chemical (USA).

2.2 Apparatus

pH measurements were made with a Mettler Toledo Seven Multi pH-ion meter. The imprinted beads were characterized using Field Emission Scanning Electron Microscopy (FESEM, ZEISS Ultraplus). HD 2070, BANDELIN, (Germany) was used for the homogenization process. MPW-251, MPWMed-Instruments (Poland) was used for centrifugation in the study.

2.3 Synthesis of Parathion-Imprinted and Non-Imprinted Polymers

N-methacryloyl-L-serine monomer, MA-Serine, was synthesized according to the previously published procedure[41]. Briefly, 0.56 g of L-Serine amino acid was dissolved in the solvent containing 1 N NaOH for 10 minutes while stirring with a magnetic stirrer. In parallel, 1 g of methacryloyl benzotriazole (MA-Bt) was dissolved in 20 mL of 1,4-dioxane with stirring, and this solution was added dropwise to the L-Serine solution. The synthesis reaction of the MA-Serine is shown in Fig. 3.

After the reaction was completed, the 1,4-dioxane was removed by evaporation. The benzotriazole, which did not react, was eliminated by extraction with ethyl acetate. Hydrochloric acid was added to the water phase until pH 5.5 and the solvent in the ambient was evaporated to obtain MA-Serine monomer.

The parathion-imprinted polymers were obtained according to the published procedure[42]. An emulsion polymerization technique was used in the published procedure. Small sized particles with a large surface area can be obtained by emulsion polymerization. Two separate phases were prepared for the emulsion polymerization technique. These are the water phase and the organic phase. To obtain the organic phase, 9 mmol of EDMA, 5 mmol of MA-Serine, 30 mg of AIBN and 80 μL of hexadecane were mixed. This mixture was then left in the ultrasonic bath for 10 minutes. 0.5 mmol of parathion and 38.5 mg of SDS were dissolved in 13 mL of water to obtain an aqueous phase. Then, the water phase and the organic phase were mixed. This process was carried out drop-wise very slowly. For minimum emulsification, the organic phase-water phase mixture was homogenized at 25.000 rpm with the homogenizer. Polymerization was carried out for 18 h at 65 °C in a water bath. After 18 hours of standing, the parathion -imprinted polymers were exposed three times to water and three times to ethanol. Thus, the monomer, surfactant, and initiator were removed.

To extract the template, incubation was carried out for 2 hours in KOH. The template was then extracted by centrifugation. For each step, the centrifuge was applied for 30 minutes at 30,000 rpm. After centrifugation, the beads were dispersed into the wash solution.

In the synthesis of the unprinted polymer, the same method as in the parathion printed polymer described in the previous heading was used. However, parathion, the target molecule, was not used in the polymerization reaction to obtain the unprinted polymer.

The preparation methods of the non-imprinted polymer and the parathion-imprinted polymer are given in Fig. 4.

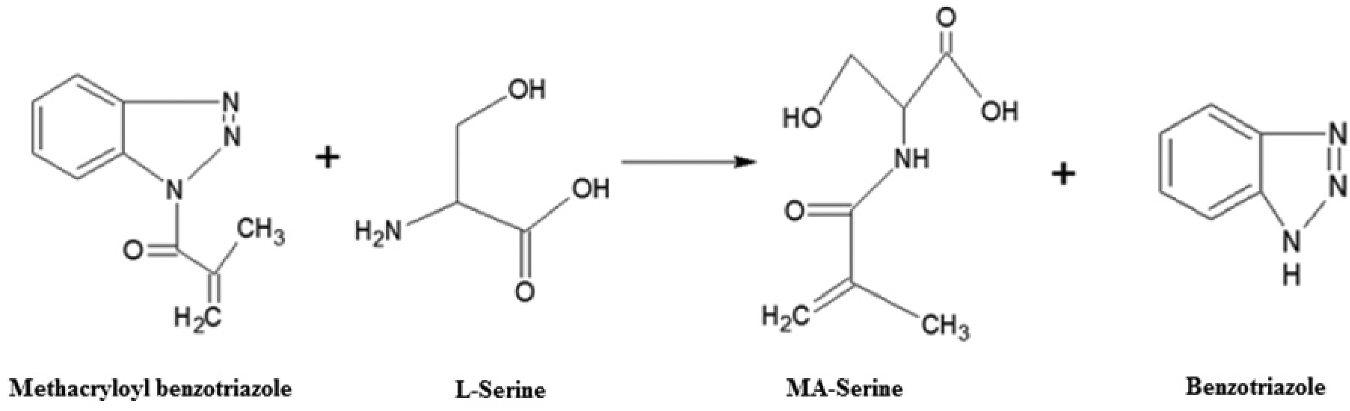


Figure 3. The synthesis reaction of the MA-Serine.

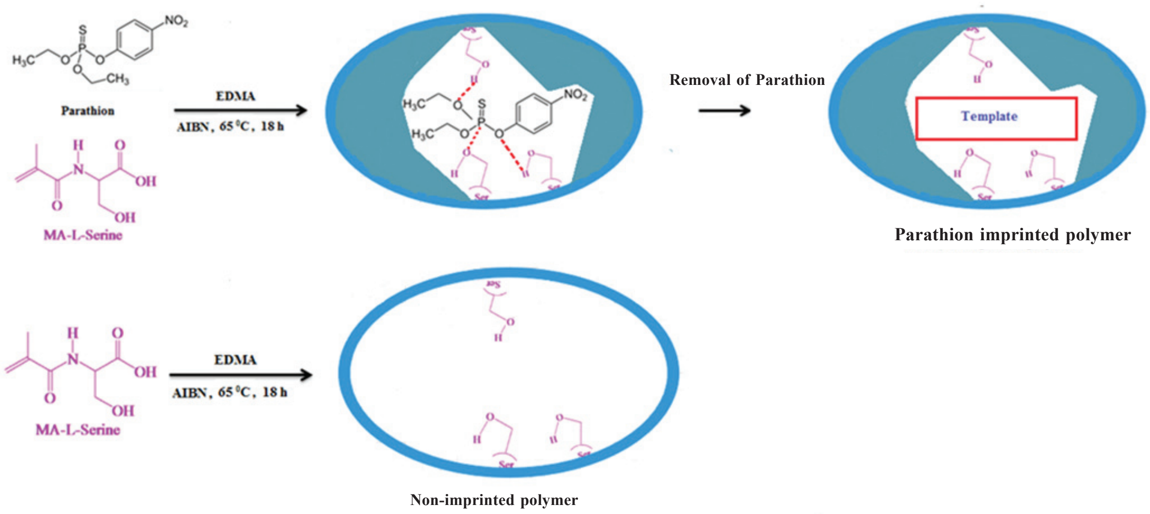


Figure 4. Scheme for the preparation of non-imprinted polymer and MIP.

2.4 Preparation of Sensor

The recognition layer of the electrode used in the potentiometric sensor was developed using the carbon paste preparation technique. Carbon paste is obtained by mixing the MIP (or NIP) with graphite powder. The mixture prepared in this study was obtained using 5 mg MIP, 100 µL DBP and 40 mg graphite powder. The resulting mixture was mixed for 10 minutes to obtain homogeneity. A copper wire was passed through a Pyrex glass tube to provide electrical conductivity. The paste was prepared as the sensing layer was filled at the end of the glass tube.

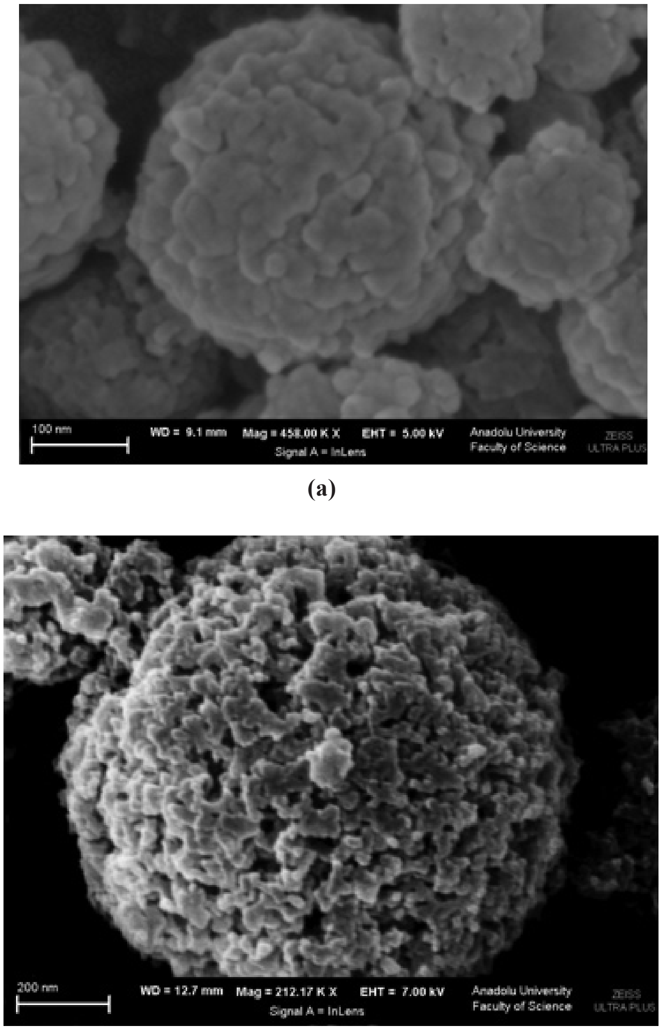
2.5 Adsorption Studies of Parathion

Conditioning was performed after the electrode was prepared. For this purpose, $3.43\text{x}10^{-7}$ molL^{-1} parathion, 0.1 M KCl, and 0.1 M KOH solutions were used. The electrode was kept in each solution for 1 hour. Every five minutes a measurement was taken to determine the time the potential was stabilized. These times were determined that 30 minutes for parathion, 35 minutes for KOH and 45 minutes for KCl. Then the parathion solutions at different concentrations were used to examine the responses of the potentiometric sensor. The parathion solutions were prepared in the range of $3.43\text{x}10^{-8}$ to $6.86\text{x}10^{-4}$ molL^{-1}. Measurements were carried out throughout the working range with the developed potentiometric sensor.

3. RESULTS AND DISCUSSION

3.1 Characterization of Nanoparticles

The imprinted beads were characterized by zeta-sizer, FESEM, and FT-IR measurements. The size of the parathion imprinted particles was determined by Zeta Sizer using a 30 μgmL^{-1} suspension in water, and parathion imprinted polymers have an average particle size of 370 nm. Figure 5 shows the morphological structures of the beads. The sizes of the beads vary from 180-420 nm. When the SEM images were examined, it was seen that the surface morphology of the beads changed after the removal of the template (Figure 5b). Measurements were taken after the sample preparation processes were completed for the FTIR analysis. When Figure 5c is examined, bands specific to and characterization of the synthesized polymer are seen (CH band (2957 cm^{-1}), carboxylic acid band (3441 cm^{-1}), carbonyl band (1730 cm^{-1})).



(a)

(b)

Figure 5. (a) SEM picture of MIP and NIP (b) Nanoparticles.

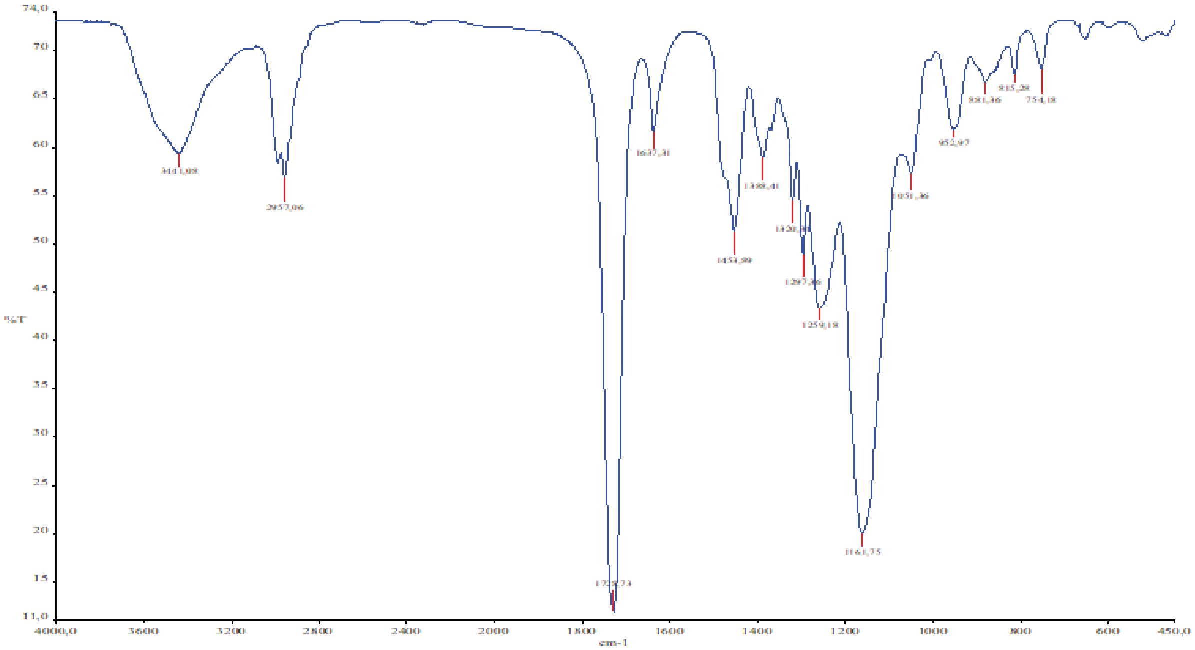


Figure 5(c). FT-IR spectra of parathion imprinted beads.

3.2 Effect of pH

To determine the working pH, pH 2-12 phosphate buffer solutions containing 3.43x10^{-5} molL^{-1} parathion were prepared. The potential change as a function of pH was then plotted on the graph (Fig. 6). When the graph is examined, it is seen that the optimum pH value is obtained at approximately 7.4. For this reason, the analyses were performed using HEPES buffer (pH: 7.4).

3.3 Calibration Range

At different concentrations, parathion solutions were used to examine the responses of the potentiometric sensor. Parathion samples were prepared at increasing concentrations for analysis. When the measured potential values were transferred to the calibration graph (Fig. 7), a wide linear concentration range was observed.

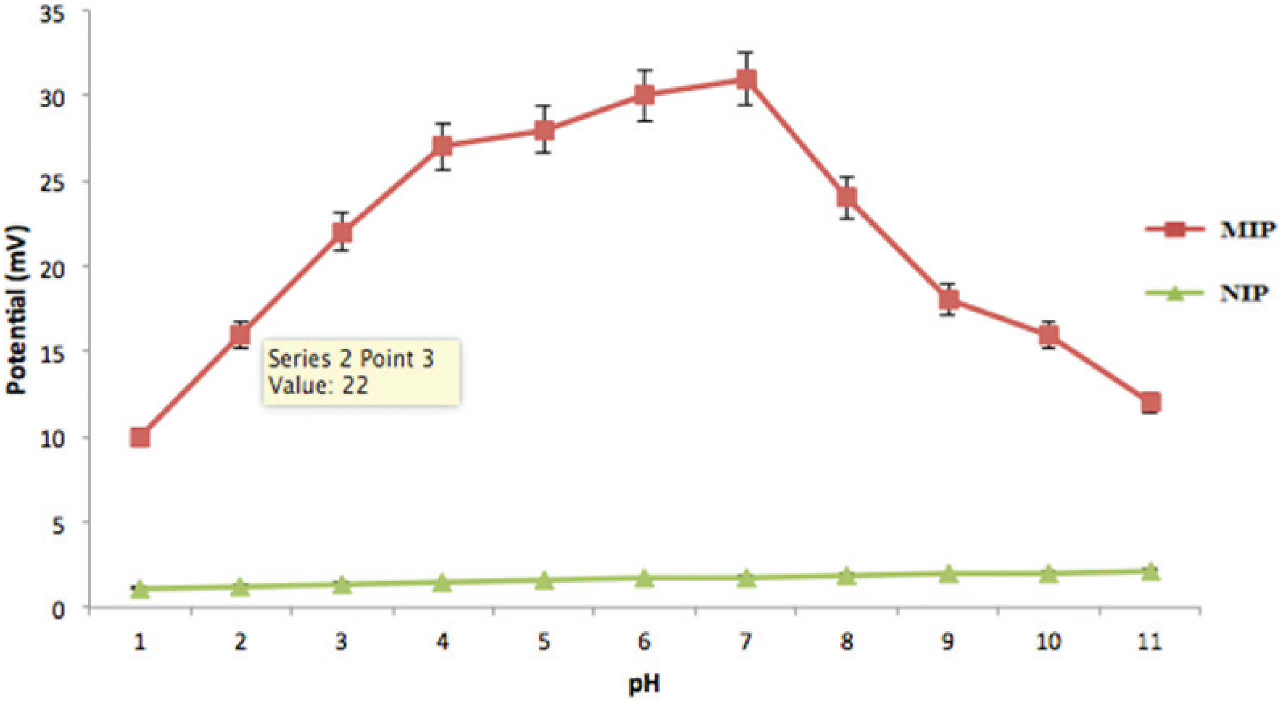


Figure 6. The effect of pH change on analysis performance. (C:3.43x10^{-5} molL^{-1}, T: 25°C, n=3).

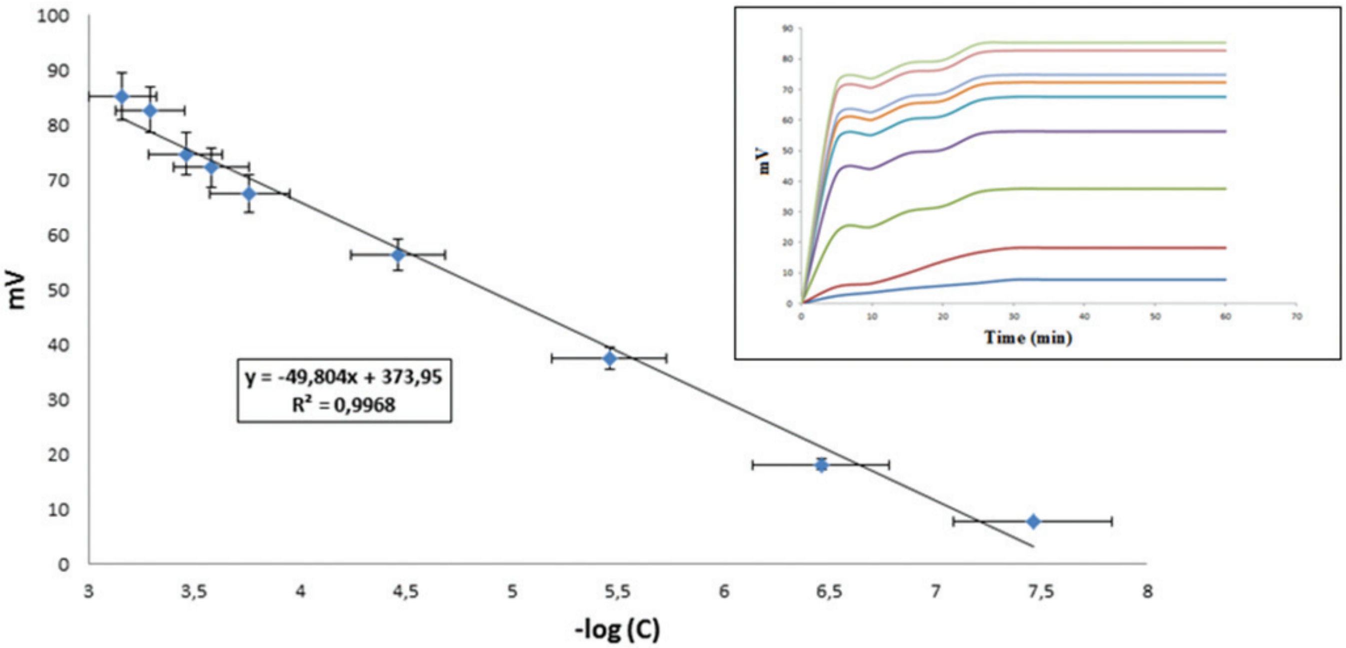


Figure 7. Calibration curve for potentiometric sensor (pH: 7.4, T: 25 °C).

When the calibration graph is examined, it is seen that the regression coefficient is 0.9968. As a result of the analysis for calculating the detection limit by using the calibration curve, the detection limit was calculated as 1.86×10^{-8} molL^{-1}. The developed MIP-based potentiometric sensor was found to have a very low detection limit. It is considered that the most important factor affecting the detection limit performance is the conductivity of the electrode. The performance of the sensor developed in this study is compared with other examples in the literature in Table 1. Compared to the sensor systems in the literature, it is seen that the performance of the sensor we developed is higher. Studies have been started to determine the response time after determining our sensor's detection limit. Parathion solutions ranging from 3.43x10^{-8} to 6.86x10^{-4} molL^{-1} were used in the measurements. The electrode we developed in our study completes its analysis of the analyte in approximately 20 seconds. This period is very short. The sensors were prepared under the same conditions to determine their reusability and treated with parathion solutions. After determining the response time of our potentiometric sensor, its reusability was examined. The analysis has shown that the sensor in question can be used repeatedly without any change in measurement performance. When the usage time of the electrode is examined, it is seen that the electrode, which is kept under the necessary storage conditions, can be used without changing its performance even after 2 months.

3.4 Selectivity

The paraoxon has been used as an analyte for detecting the selectivity of the sensor we have developed. The molecular structure of paraoxon is similar to that of parathion and is used for selectivity analysis. Potential measurements for different concentrations of paraoxon have been taken. Measured potential values for different concentrations of paraoxon are given in Table 2.

Table 1. Comparison of sensor performances

Method	DL.(mol L^1)	Linear Concentration range (mol L^1)	Reference
Voltammetric sensor	5 x 10^{-8}	0 – 4x10^{-5}	(43)
Quartz Crystal Microbalance	5 x 10^{-8}	0 – 5.1x10^{-6}	(44)
Carbon nanotube modified electrode	6.7 x 10^{-8}	0 – 2.0x10^{-7}	(45)
Amperometric sensor	5 x 10^{-5}	0 – 8x10^{-5}	(46)
MIP	1.86 x 10^{-8}	0 – 6.86x10^{-4}	This work

Table 2. Potential measurements of samples containing paraoxon at different concentrations

Molarity (mol L^{-1})	Potential (mV)
3.5×10^{-8}	-1.5
3.5×10^{-7}	4.3
3.5×10^{-6}	9.1
3.5×10^{-5}	12.2

The measurement results of the paraoxon are shown in Table 3. Examining Table 3, it is seen that the potential values of parathion are very high compared to paraoxon. While the potential value measured for 0.01 ppm parathion is 7.8 mV, the paraoxon potential at the same concentration is 1.5 mV. The selectivity coefficient of the sensor we developed was calculated using the method recommended by IUPAC[47,48]. The potentiometric selectivity coefficient value of the electrode was calculated as 1.148×10^{-4}. Therefore, the potentiometric sensor shows high selectivity against parathion.

3.5 Interference Effect

In the analysis for the interference effect, paraoxon, which is in the same family of molecules as parathion, was used in the analysis. The samples used in the interference effect study are shown in Table 3.

Table 3. Prepared samples

Parathion		Paraoxon		
ppm	mL	ppm	mL	Ratio
2	1	2	1	1:1
2	1	10	1	1:5
2	1	20	1	1:10

The potential of the sample prepared in a 1 to 1 ratio was measured at 41.4 mV. The potential of the sample prepared in a 1 to 5 ratio was measured at 40.8 mV. And the potential of the sample prepared in a 1 to 10 ratio was measured at 40.3 mV. The interference effect was calculated as 0.46 %, 3.25 %, and 5.58 %, respectively. When the measurement results are interpreted, it shows that the potentiometric sensor we developed for parathion can analyze even in sample environments containing parathion-like molecules.

3.6 Comparison of Non-imprinted Polymers with MIP

When developing a parathion selective electrode, we obtained parathion imprinted polymers by the MIP method and used it as a recognition layer on the electrode. Then, the polymers obtained by the NIP method were used as the recognition layer in the potentiometric sensor for the investigation of the sensitivity to parathion. The results obtained by the NIP method are given in Table 4.

The results show that the parathion-imprinted polymers show selectivity for the target molecule. Polymers obtained by the NIP method cannot bind to parathion, so there is no change in potential.

Table 4. Measurements were taken with recognition layer prepared with NIP

Molarity (mol L^{-1})	mV
3.43×10^{-8}	-2.8
3.43×10^{-7}	-2.6
3.43×10^{-6}	-2.7
3.43×10^{-5}	-2.1
1.72×10^{-4}	-2.4
2.61×10^{-4}	-2.5
3.43×10^{-4}	-2.3
5.14×10^{-4}	-2.6
6.86×10^{-4}	-2.4

3.7 Analysis of Tap Water Samples

The sensor we developed was also evaluated in the real matrix environment. Then, parathion was added in varying concentrations to the prepared tap water samples, and then analysis was conducted with the developed sensor. The results are given in Table 6. and the recoveries for the determination of parathion were found to be between 99.8 %, 98.6 %, and 97.3 %. When the analysis results are examined, it has been shown that the sensor we developed in this study can perform analysis even in a dense matrix environment such as tap water.

3.8 Analysis of Lake Water Samples

After the analysis studies we carried out for the parathion in the martiks environment of tap water, the analysis study was started in the lake water environment. As the lake water, samples were taken from Küçükçekmece Lake in Istanbul. Analysis results are shown in the table below. Recovery

Table 5. Detection of parathion in tap water samples spiked with different amounts of parathion (n=3)

Sample	The concentration of added parathion (M)	The concentration of found parathion (M)	Recovery (%)
Tap water 1	1.00×10^{-2}	$9.98 \times 10^{-3} \pm 1.0 \times 10^{-4}$ (RSD: % 0.98)	99.8
Tap water 2	1.00×10^{-4}	$9.86 \times 10^{-5} \pm 3.05 \times 10^{-6}$ (RSD: % 3.09)	98.6
Tap water 3	1.00×10^{-6}	$9.73 \times 10^{-7} \pm 1.9 \times 10^{-8}$ (RSD: % 1.95)	97.3

Table 6 . Detection of parathion in lake water samples spiked with different amounts of parathion (n=3)

Sample	The concentration of added parathion (M)	The concentration of found parathion (M)	Recovery (%)
Lake water 1	1.00×10^{-2}	$9.63\times10^{-3} \pm 1.84\times10^{-4}$ (RSD: %1.91)	96.3
Lake water 2	1.00×10^{-4}	$9.57\times10^{-5} \pm 1.14\times10^{-6}$ (RSD: %1.19)	95.7
Lake water 3	1.00×10^{-6}	$9.49\times10^{-7} \pm 1.97\times10^{-8}$ (RSD: %2.07)	94.9

values for parathion determination in lake water matrix were calculated as 96.3 %, 95.7 % and 94.9 %, respectively. When the analysis results are examined, it has been shown that the sensor we developed in this study can perform analysis even in a dense matrix environment such as lake water.

4. CONCLUSION

In this study, it is aimed to develop a potentiometric sensor using molecularly imprinted polymer as the sensing layer for the analysis of parathion, a nerve agent simulant, in different matrix environments. Since parathion is very similar to nerve agents (especially sarin gas) in terms of its molecular structure and mechanism of action, it is considered that the analysis methods developed for parathion can also be used for nerve agents. The sensor we developed gave very good results in terms of potentiometric performance. Our developed MIP-based potentiometric sensor showed high selectivity against the parathion molecule. In addition, when the performance characteristics of the sensor we developed are examined, it is seen that it has a very wide linear analysis range and has a much lower amount of parathion detection limit (1.86×10^{-8} molL^{-1}) compared to other methods. Studies have been carried out to determine the analysis performance of our potentiometric sensor in a dense matrix environment. Even in tap water and lake water environments, the electrode we developed continued to analyze the parathion in the sample with very high performance. In terms of interference effect, analyzes were made in the sample environment with chemicals that are very similar in molecular structure to parathion. The results showed that our potentiometric sensor system can analyze without being affected by interference. As a result of the studies carried out in terms of analysis time, it has been observed that the analysis time (20 s) of our sensor is quite low. Compared with similar studies in the literature, it is considered that the method we developed can be preferred due to advantages such as analysis time, selectivity, detection limit, reproducibility, not being affected by interference and being portable.

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CONTRIBUTOR

Dr Ozan Yağmuroğlu is currently working as an assistant professor at the Department of Chemistry, Turkish Air Force Academy. He completed his PhD in analytical chemistry. He has written many scientific articles in his field and made oral presentations at international congresses. Dr Ozan Yağmuroğlu also holds the rank of Captain in the Turkish Air Force.