

A New Potentiometric Sensor for Rapid Determination of Captopril in Pharmaceutical Formulation and Biological Samples

Parvin Pourhakkak¹, Mohammad Ali Karimi^{1*}, Hossein Tavallali¹,
Puran Pourhakkak¹, Mohammad Mazloum Ardakani²

1. Department of Chemistry, Payame Noor University, Tehran, Iran

2. Department of Chemistry, Faculty of Science, Yazd University, Yazd, 89195-741, Iran

Received: 23 April 2022

Accepted: 11 July 2022

DOI: 10.30473/ijac.2022.63786.1234

Abstract

A new potentiometric sensor based on a β -cyclodextrin modified carbon paste electrode (CPE) was designed for the determination of the captopril drug. The effect of various cyclodextrins (α , β and γ - cyclodextrins) and their percentage, binder agent and ion additive on the potential response have been investigated and the electrode with the best potential response was found. The linear concentration range for this electrode was 7.0×10^{-7} - 1.0×10^{-1} M with a low detection limit of 2.0×10^{-7} M. The effect of pH and temperature on the Nernstian slope was also investigated and the optimal range was obtained. The selectivity of the captopril CPE to interfering species including Li^+ , K^+ , Ni^+ , Mg^{2+} , Ca^{2+} , Co^{2+} , Cr^{2+} , Cr^{3+} , Zn^{2+} , Mn^{2+} , Fe^{2+} , F^- , Cl^- , SO_4^{2-} , $\text{C}_2\text{O}_4^{2-}$, PO_4^{3-} , $\text{C}_2\text{O}_4^{2-}$, ascorbic acid, uric acid, glucose, D-fructose and sucrose was determined by Separate Solution (SSM) and Matched Potential Method (MPM) methods. Finally, the proposed electrode was tested for measuring captopril in drug formulation, blood serum, and urine samples.

Keywords

Potentiometric Sensor; Captopril; Modified Carbon Paste Electrode; β -Cyclodextrin; Ion-Selective Electrode.

1. INTRODUCTION

Captopril with the chemical name 1 - [(2S) -3-mercapto-2-methylpropionyl] -L-proline (CPT, Fig. 1) is one of the drugs used to regulate and reduce blood pressure and treat heart failure and congestion.

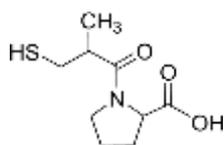


Fig. 1. Molecular structure of captopril

This drug impedes the angiotensin-converting enzyme and by this means shows its action. Various analytical methods have been used for captopril analysis in pharmaceutical formulations, including capillary electrophoresis [1], high-performance liquid chromatography (HPLC) [2], polarography [3], voltammetry [4], coulometry [5], Amperometry [6], conductivity [7], fluorometry [8], colourimetry [9] and flow injection methods [10]. Some of these methods are not simple and their analysis requires expensive or complex devices. Potentiometric techniques with ion-selective membrane electrodes (ISE) are a simple and valuable tool for captopril analysis in pharmaceutical formulations because they can directly measure active ions in the solution. ISEs are affordable, easy to use and maintain ISEs, and

simple, fast and accurate methods make them very suitable for the analysis of pharmaceutical products [11]. Various sensors based on carbon paste electrodes have been developed for the determination of captopril some of them were listed in Table 1.

Carbon paste electrode is relatively inexpensive and relatively easy to prepare and has become one of the most popular electrode materials used for laboratory preparation of various electrodes, sensors and detectors. Chemical inertia, strength, renewability, stable response, low ohmic resistance, no requirement for an internal solution, and the usefulness of carbon paste electrodes make it appropriate for a variety of measurement and diagnostic applications. Chemically modified electrodes must increase the speed of electron transfer by reducing the excess voltage. Studies have shown that chemically modified electrodes increase electron transfer rate by reducing excess voltage, amplifying response signals, and improving sensitivity and reproducibility [12]. Cyclodextrins are a good host environment for interacting with guests due to their hydrophobic cavity. The outer part of cyclodextrins is soluble in water and allows hydrogen interactions with the solvent. β -cyclodextrin with good water solubility and biocompatibility is an ideal candid for drug loading and complexation due to its full pore size, availability, and relatively low cost [13].

*Corresponding Author: ma_karimi43@yahoo.com

Table 1. Comparison of the reported CPE with the used techniques for captopril analysis.

Electrode	Modifier	Method	Detection limit (μM)	Linear range (μM)	Ref.
CPE	salophen complexes of cobalt(III) perchlorate	DPV	0.05	0.1 to 100	[17]
CPE	ferrocene dicarboxylic acid	SWV	0.091	0.3–1400	[18]
MWCNPE	p-aminophenol	SWV	0.02	0.05 to 0.5 and 0.5 to 50.0	[19]
CPE	(E)-3-((2-(2,4-dinitrophenyl)hydrazono)methyl)benzene-1,2-diol (DHB) and carbon nanotubes (CNTs)	DPV	0.07	0.2–800.0	[20]
CPE	copper–cobalt hexacyanoferrate	SWV	4.2	$(5.0–31) \times 10^{-6}$	[21]
CPE	carbon nanotube and benzoylferrocene	SWV	0.03	0.4 to 350	[22]
ZnO/CNT/CPE	N-(4-hydroxyphenyl)-3,5-dinitrobenzamide	SWV	0.01	0.05–800	[23]
CPE	NiO NPs/NPS	SWV	0.007	0.035 to 550	[24]
CNPE	isoproterenol	SWV	0.1	0.3 to 90	[26]
CPE	ferrocene carboxaldehyde and ZnO nanoparticle	SWV	0.04	0.08–500.0	[26]
CPE	cyclotricatechylene				
CPE	NiO/CNTs and (2-(3,4-dihydroxyphenethyl)isoindoline-1,3-dione)	SWV	0.009	0.07–200.0	[27]
CPE	1, 1'-bis(2-phenylethan-1-ol)ferrocene	SWV	0.05	0.09–450.0	[28]
CPE	rutin		89.4	20 to 1000	[29]
CPE	gold nanoparticles/biphenol–biphenquinone	DPV	0.0004	0.001–0.15 and 0.15–50.0	[30]
CPE	β -Cyclodextrin	Potentiometry	0.20	0.7–100000	In this work

MWCNPE: multiwall carbon nanotubes paste electrode; CPE: carbon nanotubes paste electrode

SWV: Square Wave Voltammetry; DPV: Differential Pulse Voltammetry

DED: (9,10-dihydro-9,10-ethanoanthracene-1,12-dicarboximido)-4-ethylbenzene-1,2-diol

CV: cyclic voltammetry

In this research, a carbon paste electrode modified with a β -cyclodextrin ion carrier has been used as a useful analytical tool for measuring captopril in different samples. The potential responses of the electrode were measured for α , β and γ cyclodextrin and the best response was selected. The effect of cyclodextrin percentage and various binder agents were also investigated. Finally, the selectivity coefficient of the sensor was studied in the blood serum sample and spiked urine.

2. EXPERIMENTAL

2.1 Apparatus

A glass cell containing carbon paste as the working electrode and Ag/AgCl as the reference electrode (Ag/AgCl|KCl(sat'd)|Test solution| carbon paste| cell) was used for the measurement of potential. In addition, a potentiometer/pH device of ZAG Industrial Chemicals (model 162) was employed to record the potential and pH. A Metrohm pH meter

and a magnetic stirrer (ZAG Shimi, Iran) Iran were applied to perform the experiments.

2.2. Reagents

Graphite powder with a particle size lower than 50 μm (Merck) and density of approximately 2.2 g cm^{-3} along with mineral oil (Nujol, Aldrich) with high purity was used to prepare carbon paste. α , β and γ Cyclodextrins ionophores, bis-(2-hydroxyethyl) phthalate (BEHP), ortho-nitrophenyl octyl ether (2-NPOE), dioctyl sebacate (DOS), dioctyl phthalate (DOP), dibutyl phthalate (DBP), potassium tetrakis (p-chlorophenyl) borate (KTPCIPB) or trioctyl dodecyl ammonium chloride (TDAC-Cl) binder agents were purchased from Merck company.

2.3. Carbon paste electrode preparation

To organize the carbon paste electrode (CPE), first graphite powder and β -CD with a certain percentage were thoroughly mixed in a mortar.

Nujole oil or other binder agents was then added to it and the resultant mixture was crushed for at least half an hour to receive a homogeneous paste. In some cases, KTPCIPB or TDACI-Cl ion additive as an electroactive material was added to improve the electrode response (electrodes No. 4 and 10-18). The carbon paste was then inserted into the end of a 2 mm diameter and a height of 3 cm polyethylene syringe and the material inside the syringe was well packed. The carbon paste was related to the potentiometer via a copper wire in contact with its surface. The surface of the carbon paste was then rubbed with soft paper to obtain a completely smooth surface. At the end of each test, a thin piece was removed from the CPE surface with a thin cutter and rubbed again to renew the surface for the next investigation.

3. RESULT AND DISCUSSION

3.1 Optimization of components of CPE

The sensitivity, selectivity, and linear range of the carbon paste electrode depend greatly on the composition of the CPE, the properties of the binder agent and the ion additives employed. Therefore different CP compositions were prepared (see Table 2).

The impact of cyclodextrin type (ion carrier), binder agent, and their mass ratio on the potentiometric response of the designed CPE electrode was studied. To test the effect of cyclodextrin type, α , β and γ cyclodextrins were used and their response to captopril was investigated. It was observed that the best potential response to captopril was obtained by β -cyclodextrin (β CD) modified CPE (see Fig. 2).

Table 2. Electrode responses with different compositions of CPE

CPE NO.	Ion additive	Ion carrier	Plasticizer	Graphite powder	Article I. Slope (mV/decade)	Linear concentration range (M)
1	-	0.0	35.0 (Nujol)	65.0	1.12±43.8	5.0×10^{-5} - 1.0×10^{-1}
2	-	7.0	33.0 (Nujol)	60.0	1.10±55.6	1.0×10^{-6} - 1.0×10^{-1}
3	-	11.0	30.0 (Nujol)	59.0	0.84±55.8	1.0×10^{-6} - 1.0×10^{-1}
4	1.0 (TDAT-Cl)	12.0	28.0 (Nujol)	59.0	0.20± 59.6	7.0×10^{-7} - 1.0×10^{-1}
5	-	14.0	28.5 (Nujol)	57.5	0.40±56.8	1.0×10^{-5} - 1.0×10^{-1}
6	-	13.0	28.5 (Bis-EHS)	58.5	0.15±61.1	1.0×10^{-6} - 1.0×10^{-1}
7	-	11.0	31.0 (2-NPOE)	58.0	0.22±46.5	1.0×10^{-7} - 1.0×10^{-1}
8	-	12.0	30.0 (DOP)	58.0	0.25±60.7	1.0×10^{-6} - 1.0×10^{-1}
9	-	12.0	30.0 (DBP)	58.0	0.17±55.3	1.0×10^{-6} - 1.0×10^{-1}
10	1.0 (TPCTPB)	12.0	30.0 (Nujol)	57.0	0.60 ±49.6	2.0×10^{-5} - 1.0×10^{-1}
11	2.0 (TPCTPB)	12.0	29.0 (2-NPOE)	57.0	0.16±57.4	2.0×10^{-6} - 1.0×10^{-1}
12	2.0 (TDAT-Cl)	12.0	28.0 (2-NPOE)	58.0	0.10±52.7	1.0×10^{-7} - 1.0×10^{-1}
13	2.0 (TDAT-Cl)	12.0	28.0 (Bis-EHS)	58.0	0.30±49.3	1.0×10^{-6} - 1.0×10^{-1}
14	1.0 (TDAT-Cl)	12.0	34.0 (DOS)	59.0	0.10±53.2	1.0×10^{-5} - 1.0×10^{-1}
15	1.0 (TDAT-Cl)	12.0	33.0 (DOS)	59.0	0.30±53.1	1.0×10^{-6} - 1.0×10^{-1}
16	1.0 (TDAT-Cl)	12.0	35.0 (DOP)	59.0	0.20±55.0	1.0×10^{-6} - 1.0×10^{-1}
17	1.0 (TDAT-Cl)	12.0	37.0 (DOP)	59.0	0.25±55.3	1.0×10^{-6} - 1.0×10^{-1}
18	2.0 (TDAT-Cl)	12.0	29.0 (DBP)	59.0	0.30±55.6	1.0×10^{-6} - 1.0×10^{-1}

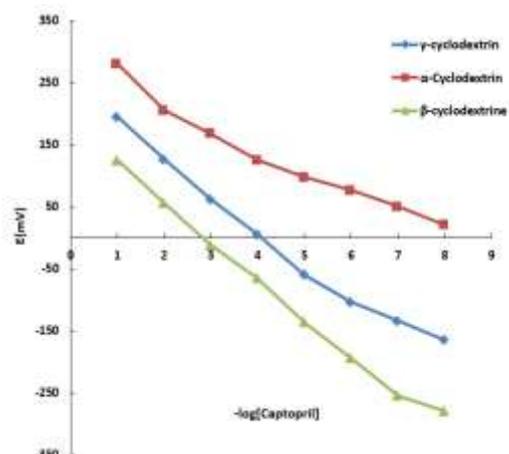


Fig. 2. Potentiometric response of an electrode made with α , β and γ -cyclodextrins.

Therefore, a calibration curve was generated for CPE- β CD at different concentrations of captopril. For the study of the effect of the mass percentage of β -CD, electrodes were made with various amounts of β -CD ion carrier and the effect of different mass ratios on the response of the electrodes was investigated (see the result in Fig. 3 and Table 2). The best-modified CPE with a Nernstian slope of $61.1 \text{ mV decade}^{-1}$ belonged to the electrode containing 13% β -CD (CPE No. 6). It was observed that the β -CD ion carrier plays a significant role in the potential response of the CPE, so without the presence of the electrode modifier, the β -CD electrode shows little response to the captopril. This is because of the improvement in the conductivity of the sensor and transduction of the chemical signal to the electrical

signal which enhances the response time and dynamic range of the working electrode.

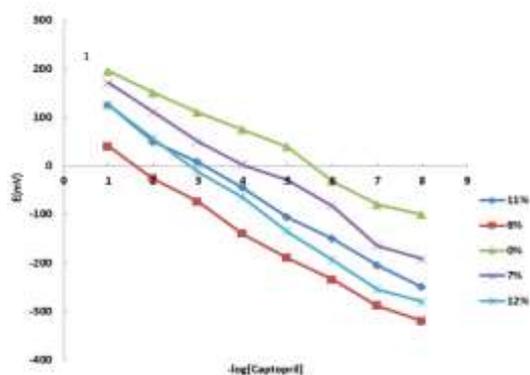


Fig. 3. Potentiometric response of electrodes made with different percentages of β -cyclodextrin ion carrier

Since the type of binder agent has a great influence on the dielectric constant of the membrane phase and the mobility of the ion carrier plays an important role in determining the properties of the electrode, the effect of the binder agent was also investigated. For this mean, the potentiometric response of CPE made with different binding agents such as DBP, Nojol, DOP, NPOE, DOS and (Bis-EHS) was investigated and the best sensitivity and linear range were obtained. The results are shown in Table 2 and Fig. 4. Experiments revealed that the carbon paste electrode made with Nujol binder agent (CPE No. 4) with a Nernstian slope of $59.6 \text{ mV decade}^{-1}$ demonstrated the best potential response to captopril and therefore, Nujol was utilized as the best binder in the following experiments.

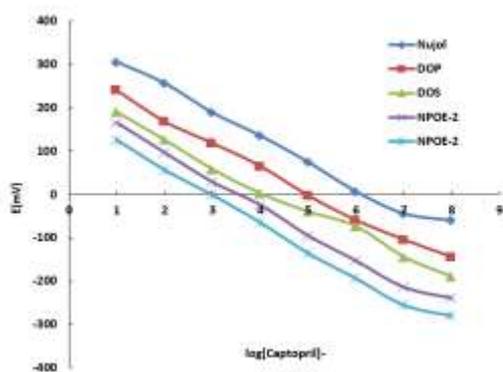


Fig. 4. Potential response of electrodes fabricated with different binder agents

Finally, the effect of two ion additives namely KTPCIPB or TDAC-Cl on the performance of the fabricated sensor was studied. It is marked that the addition of TDAC-Cl to the paste containing the Nujol binder agent increases the Nernstian slope and the best response was observed in the CPE NO. 4 (see Table 2). This trend is followed for the paste

consisting of DOP and the Nernstian slope increase with the addition of TDAC-Cl. In other samples, no regular trend is observed.

3.2 Calibration curve

The measuring range of an ion-selective electrode is the linear part obtained in the calibration graph as illustrated in Fig. 5. According to the results given in Table 2, the CPE fabricated by applying 13% of β -CD ion carrier and Nujol binder agent created the best Nernst slopes and concentration range (see Fig. 5). The linear concentration range for this electrode made by mentioned composition is 7.0×10^{-7} - 1.0×10^{-1} M which has Nernstian behaviour in this range. The detection limit derived by extrapolating the linear parts of the calibration curve is 2.0×10^{-7} M.

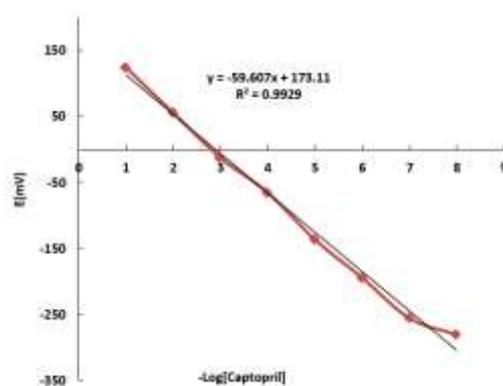


Fig. 5. Calibration curve of captopril CPE with optimal CPE composition

3.3 Response time and Lifetime of the electrode

The time required for the electrode potential to reach ± 1 mV equilibrium potential is defined as the response time. To measure the electrode response, the electrode was placed in the captopril solutions with various concentrations (1×10^{-6} to 1×10^{-2} mol L^{-1}), each solution was 10 times different in concentration. The potential change versus the time curve was plotted in Fig. 6 and Table 3. As observed, at higher concentrations, the electrode reaches equilibrium faster. The reaction time of this electrode is about 5 seconds.

Table 3. Potential response of captopril CPE in solution of captopril with a concentration of 1.0×10^{-3} for 3 hours

Potential (mV)	Time (min)	Potential (mV)	Time (min)
10	153	100	154
20	154	110	152
30	152	120	153
40	153	130	152
50	153	140	153
60	152	150	154
70	152	160	154
80	153	170	153
90	154	180	154

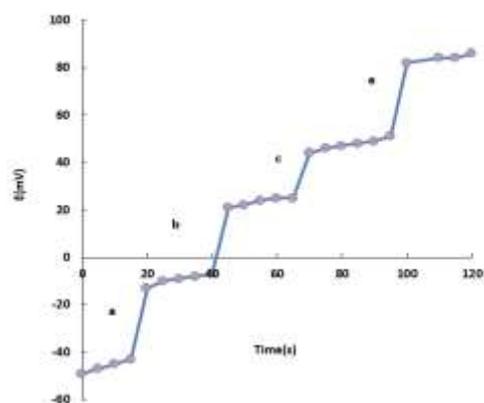


Fig. 6. The response-time curve for captopril selective electrode

To evaluate the stability of the electrode response, it was immersed in captopril solution for 3 hours at a concentration of 0.1×10^{-2} M and the potential response was recorded every 10 minutes. The standard deviation obtained during this period was 0.54 mV ($n = 18$). The small standard deviation indicates satisfactory stability of the captopril CPE response. By alternating generating the calibration diagram of one electrode for 2 months, it was found that the life of the modified CPE is more than 2 months.

The reversibility of the CPE response was also examined by alternately measuring the potential response of β -CD/CPE to the two solutions of captopril (1.0×10^{-3} M and 0.1×10^{-4} M) during the stirring and the results were given in Table 4. The low standard deviation obtained for the resulting potential difference (0.4 mV) indicates that the ion-selective electrode has good reversibility.

Table 4. Alternating potential response of captopril CPE in solutions of captopril (3×10^{-3} and 1.0×10^{-4})

E (mV) (1.0×10^{-4} M)	E (mV) (1.0×10^{-3} M)	time
1	80	120
2	80	120
3	80	118
4	78	118
5	80	120
6	78	118
7	80	120
8	80	118

3.4 The effect of pH and temperature

To investigate the effect of pH on the responsivity of the electrodes, the potential changes of the captopril solutions (1.0×10^{-3} and 0.1×10^{-4}) were recorded in the pH range of 2-13 (see Fig. 7). Hydrochloric acid or potassium hydroxide was used for the pH adjustment. The results showed that the suitable pH for optimal electrode operation is in the range of 4 to 8.5. According to the diagram, the potential response decrease at higher

pH values, which relates to the increase in the OH^- ions and the simultaneous response of the electrode to OH^- and captopril. At lower pH values, the potential response boosts due to the increase of H^+ ion, which causes the protonation of captopril and decreases its anion concentration.

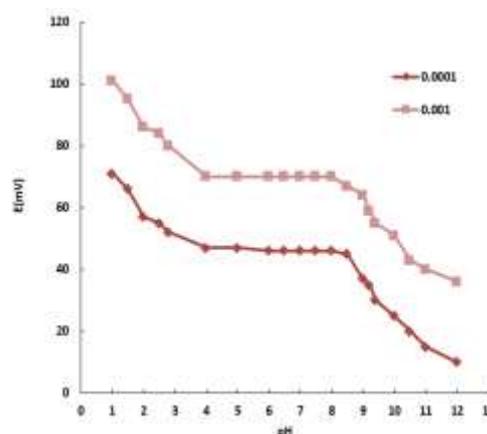


Fig. 7. Effect of pH on the response of CPE at two different concentrations of captopril

The changes in the performance of the β -CD/CPE for the experimental solution for the captopril were studied at 15 to 50 °C (see Table 5). According to the results, β -CD/CPE shows the Nernstian behaviour which indicates that the electrode can be used suitably at these temperatures. There is no change in the detection limit with an increase in the temperature but the best Nernstian slope and wide linear concentration range are observed at 50 °C.

Table 5. β -Cyclodextrine/CPE response at different temperatures

No	temperature (°C)	Concentration rang (M)	Detection limit (M)	Slope
1	15	3.0×10^{-5} - 1.0×10^{-2}	1.0×10^{-7}	57.5
2	25	5.0×10^{-5} - 1.0×10^{-2}	1.0×10^{-7}	57.1
3	35	1.0×10^{-5} - 1.0×10^{-1}	1.0×10^{-7}	58.1
4	40	2.5×10^{-5} - 1.0×10^{-2}	1.0×10^{-7}	58.3
5	50	1.0×10^{-8} - 1.0×10^{-1}	2.0×10^{-7}	59.5

3.5 Selectivity of the electrode

Selectivity coefficients of the potentiometric technique indicating the tendency of the offered electrode for interfering ions were determined by Separate Solution (SSM) and Matched Potential Method (MPM) methods. The coefficient by the SSM method is time-dependent and is defined as a linear function of time that increases to a given negative power. According to the MPM method,

the interfering ions (X) are continuously added to the reference solution (desired analyte with a certain concentration) and the potential is read. The addition of the X ions is continued until the measured potential is reached to the potential of the reference ion before adding the X ions. The selectivity coefficient is then determined by the following formulas [14]:

$$\log K_{Drug,J}^{Pot} = \frac{E_2 - E_1}{s} + \log[Drug] - \log[J^{X+}]^{1/X} \quad (1)$$

$$\log K_{Drug,J}^{Pot} = \frac{a_{Drug}}{a_J} \quad (2)$$

MPM and SSM methods were used to measure the selectivity coefficients of the electrode in a captopril solution (0.1×10^{-4} M). The coefficients obtained for the captopril electrode was shown in Table 6. The results of this table revealed that the captopril electrode to has a low selectivity to anions such as $C_2O_4^{2-}$, Na^+ , SO_4^{2-} and K^+ as well as biological compounds such as D-fructose, sucrose, ascorbic acid, glucose, uric acid. Mineral anions do not interfere due to their size, mobility, and impermeability. In the case of sugars and biological compounds, the high selectivity depends mainly on the difference in polarity and lipophilicity of the molecule relative to captopril. Therefore, the interference of these species in the measurement of captopril is negligible and captopril can be measured in the presence of these species without disturbance.

3.6 Analysis of drug samples

To analyze the drug sample, a captopril tablet containing 250.0 mg of captopril was ground

completely and 4 mg of it was dissolved in water and diluted into a 50 ml balloon. Then 1 ml of this solution with 19 ml of the buffer was transferred to a beaker and certain concentrations of captopril were prepared. The amount of captopril in the solution is then measured by the proposed electrode using the standard addition method. The results were presented in Table 7. The results show that the proposed electrode can be used successfully for measuring captopril in drug samples with a reasonable result. This is due to the low interference of the concurrence species in the tablet with the performance of the electrode. The values of recovery are consistent with the reported ones in the literature which used glass pH electrodes [8, 15].

The applicability of captopril CPE for the determination of captopril in two suitable biological matrices including blood serum samples and spiked urine was also checked. For the preparation of the samples, 5 ml of human serum (or urine) was transferred to a 50 ml balloon and phosphate buffer solution (pH =7). The solution was shaken for 5 minutes, 25 ml of this solution was then transferred to a 50 ml human, and different amounts of captopril were spiked individually into the mentioned solution. The standard addition method was employed to measure the recovery values. The results are displayed in Table 8. According to the experiments performed and comparing the obtained values with the added values, it can be concluded that the captopril carbon paste electrode can be used as a suitable measuring tool [16].

Table 6. Selectivity coefficients for captopril CPE using separate solution method (SSM) and matched potential method (MPM)

Ion (J)	K(SSM)	K(MPM)	Ion (J)	K(SSM)	K(MPM)
Na ⁺	1.9×10^{-5}	3.4×10^{-4}	K ⁺	5.0×10^{-5}	2.4×10^{-5}
Li ⁺	3.1×10^{-3}	5.6×10^{-4}	Ni ⁺	3.9×10^{-4}	6.2×10^{-4}
Mg ²⁺	8.5×10^{-4}	5.1×10^{-4}	Ca ²⁺	4.2×10^{-3}	8.5×10^{-4}
Cr ³⁺	1.7×10^{-2}	7.4×10^{-4}	F ⁻	3.4×10^{-3}	8.2×10^{-4}
Zn ²⁺	3.8×10^{-4}	5.4×10^{-4}	Co ²⁺	1.7×10^{-3}	7.3×10^{-4}
Mn ²⁺	2.0×10^{-3}	6.1×10^{-4}	Cr ²⁺	2.0×10^{-4}	5.2×10^{-4}
Fe ²⁺	2.4×10^{-3}	3.1×10^{-4}	Ascorbic acid	6.5×10^{-5}	5.3×10^{-5}
D-fructose	1.1×10^{-6}	5.1×10^{-4}	glucose	2.8×10^{-5}	6.3×10^{-5}
Sucrose	7.9×10^{-5}	4.6×10^{-5}	Uric acid	9.2×10^{-3}	7.8×10^{-3}
SO ₄ ²⁻	2.2×10^{-5}	3.2×10^{-5}	Cl ⁻	3.2×10^{-4}	1.2×10^{-5}
PO ₄ ³⁻	1.2×10^{-4}	2.2×10^{-4}	C ₂ O ₄ ²⁻	2.2×10^{-5}	4.2×10^{-5}

Table 7. Results of captopril sensing in tablets by captopril CPE sensor

Added captopril ($\mu\text{g ml}^{-1}$)	Measured captopril ($\mu\text{g ml}^{-1}$)	Recovery (%)
0.5	0.52 ± 0.01	102.0
5.00	5.08 ± 0.07	101.4
20.00	19.83 ± 0.04	99.2

Table 8. Results of captopril sensing in plasma and urine by captopril CPE sensor

sample	Added captopril (M)	Measured captopril (M)	Recovery (%)
plasma	1.00×10^{-3}	$0.99 (\pm 0.03) \times 10^{-3}$	98.75
	1.00×10^{-4}	$0.97 (\pm 0.04) \times 10^{-4}$	96.97
	1.00×10^{-5}	$1.02 (\pm 0.05) \times 10^{-5}$	10.325
urine	1.00×10^{-3}	$0.97 (\pm 0.04) \times 10^{-3}$	96.75
	1.00×10^{-4}	$0.98 (\pm 0.05) \times 10^{-4}$	97.87
	1.00×10^{-5}	$1.06 (\pm 0.04) \times 10^{-5}$	106.25

The application of analytical selective electrodes was tested to determine the amount of captopril in various biological and pharmaceutical samples. The proposed electrode was used as an indicator electrode in the titration of 25 ml of 0.1×10^{-3} M captopril solution with a solution of sodium tetraphenylborate with a concentration of 0.1×10^{-2} M. The results showed that this electrode can be used for captopril potentiometric titration endpoint identification (see Fig. 8).

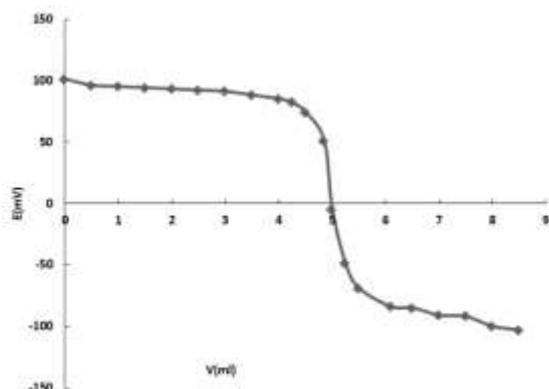


Fig. 8. Captopril titration of 25 ml of 0.1×10^{-3} M captopril solution with a solution of sodium tetraphenylborate with a concentration of 0.1×10^{-2} M.

4. CONCLUSION

A novel potentiometric sensor established on a carbon paste electrode modified with β -cyclodextrin was designed for the determination of the captopril drug. The CPE fabricated by applying 13% of β -CD ion carrier and Nujol binder agent created the best Nernst slopes and concentration range. The linear concentration range for this electrode was 7.0×10^{-7} - 1.0×10^{-1} M and a low detection limit of 2.0×10^{-7} M. The results showed the suitable pH for optimal electrode operation is in the range of 4 to 8.5. The reaction time of this electrode is about 5 seconds. The suggested captopril electrode has a very suitable selectivity to anions such as F^- , Cl^- , SO_4^{2-} , PO_4^{3-} and $C_2O_4^{2-}$ as well as biological compounds such as glucose, glycine, cytosine, lactose, urea and drugs such as metformin, ibuprofen, fluvoxamine. The proposed electrode can be used successfully for measuring captopril in drug formulation, blood serum, and urine samples. Finally, the noted electrode can also

be used for captopril potentiometric titration endpoint identification

REFERENCES

- [1] S. Hillaert, W. Van den Bossche, Determination of captopril and its degradation products by capillary electrophoresis, *J. Pharm. Biomed.*, 21 (1999) 65-73.
- [2] V. Cavrini, R. Gotti, V. Andrisano, R. Gatti, 1, 1'-[Ethenylenedibis (sulfonyl)] bis-benzene: A useful pre-chromatographic derivatization reagent for HPLC analysis of thiol drugs, *Chromatographia*, 42 (1996) 515-520.
- [3] J. Fraga, A. Abizanda, F. Moreno, J. Leon, Application of principal component regression to the determination of captopril by differential pulse polarography with no prior removal of dissolved oxygen, *Talanta*, 46 (1998) 75-82.
- [4] K. Sarna, Z. Fijalek, Voltammetric and electrochemical quartz crystal microbalance study of antithyroid drugs, *Chemia analityczna*, 42 (1997) 425-433.
- [5] K. Nikolic, K. Velasevic, Coulometric determination of captopril, *Acta Pol. Pharm.*, 48 (1991) 5-5.
- [6] M.E. Mohamed, H.Y. Aboul-enein, Amperometric and conductimetric methods for simultaneous determination of captopril and bendroflumethiazide, *Anal. Lett.*, 18 (1985) 2591-2603.
- [7] Y. Umezawa, P. Bühlmann, K. Umezawa, K. Tohda, and S. Amemiya, *Pure and Applied Chem.* 72 (2000) 1851.
- [8] P.d.S. Ribeiro, A. Santini, H.R. Pezza, L. Pezza, Potentiometric determination of captopril in pharmaceutical formulations, *Eclética Quím.*, 28 (2003) 39-44.
- [9] R.S. Guerrero, S.S. Vives, J.M. Calatayud, Fluorimetric determination of captopril by flow injection analysis, *Microchem. J.*, 43 (1991) 176-180.
- [10] C. Sastry, A. Sailaja, T.T. Rao, Determination of captopril by two simple spectrophotometric methods using oxidative coupling reaction, *Die Pharmazie*, 46 (1991) 465.
- [11] Z.D. Zhang, W.R.G. Baeyens, X.R. Zhang, G. Van der Weken, Chemiluminescence flow-

- injection analysis of captopril applying a sensitized rhodamine 6G method, *J. Pharm. Biomed.*, 14 (1996) 939-945.
- [12] R.-I. Stefan, J.K.F. van Staden, H.Y. Aboul-Enein, A new construction for a potentiometric, enantioselective membrane electrode—its utilization to the S-captopril assay, *Talanta*, 48 (1999) 1139-1143.
- [13] S. Tajik, H. Beitollahi, F.G. Nejad, M. Safaei, K. Zhang, Q. Van Le, R.S. Varma, H.W. Jang, M. Shokouhimehr, Developments and applications of nanomaterial-based carbon paste electrodes, *RSC Advances*, 10 (2020) 21561-21581.
- [14] B. Gidwani, A. Vyas, A comprehensive review on cyclodextrin-based carriers for delivery of chemotherapeutic cytotoxic anticancer drugs, *Biomed Res. Int.*, 2015 (2015).
- [15] S. Khalil, A. Kelzieh, and S. A. Ibrahim, Ion-selective electrode for the determination of prazosin in tablets, *J. Pharm. Biomed. Anal.*, 33 (2003) 825.
- [16] H. Ibrahim, Y. M. Issa, and H. M. Abu-Shawish, Potentiometric flow injection analysis of dicyclomine hydrochloride in serum, urine and milk, *Anal. Chim. Acta*, 532 (2005) 79.
- [17] S. Shahrokhian, Z. Kamalzadeh, A. Bezaatpour, D.M. Boghaei, Differential pulse voltammetric determination of N-acetylcysteine by the electrocatalytic oxidation at the surface of carbon nanotube-paste electrode modified with cobalt salophen complexes, *Sens. Actuators B Chem.*, 133 (2008) 599-606.
- [18] H. Karimi-Maleh, A. Ensafi, A. Allafchian, Fast and sensitive determination of captopril by voltammetric method using ferrocenedicarboxylic acid modified carbon paste electrode, *J. Solid State Electrochem.*, 14 (2010) 9-15.
- [19] A.A. Ensafi, B. Rezaei, Z. Mirahmadi-Zare, H. Karimi-Maleh, Highly selective and sensitive voltammetric sensor for captopril determination based on modified multiwall carbon nanotubes paste electrode, *J. Braz. Chem. Soc.*, 22 (2011) 1315-1322.
- [20] M. Mazloum-Ardakani, M.A. Sheikh-Mohseni, B.-F. Mirjalili, L. Zamani, Simultaneous determination of captopril, acetaminophen and tryptophan at a modified electrode based on carbon nanotubes, *J. Electroanal. Chem.*, 686 (2012) 12-18.
- [21] F. Jalali, S. Ranjbar, Electrocatalytic oxidation of captopril using a carbon-paste electrode modified with copper-cobalt hexacyanoferrate, *Russ. J. Electrochem.*, 50 (2014) 482-489.
- of captopril in pharmaceutical and biological samples, *Measurement*, 47 (2014) 770-776.
- [23] H. Bagheri, H. Karimi-Maleh, F. Karimi, S. Mallakpour, M. Keyvanfard, Square wave voltammetric determination of captopril in liquid phase using N-(4-hydroxyphenyl)-3, 5-dinitrobenzamide modified ZnO/CNT carbon paste electrode as a novel electrochemical sensor, *J. Mol. Liq.*, 198 (2014) 193-199.
- [24] H. Karimi-Maleh, M. Moazampour, V.K. Gupta, A.L. Sanati, Electrocatalytic determination of captopril in real samples using NiO nanoparticle modified (9, 10-dihydro-9, 10-ethanoanthracene-11, 12-dicarboximido)-4-ethylbenzene-1, 2-diol carbon paste electrode, *Sens. Actuators B Chem.*, 199 (2014) 47-53.
- [25] H. Krimi, M. Keyvanfard, K. Alizad, Voltammetric determination of captopril using multiwall carbon nanotubes paste electrode in the presence of isoproterenol as a mediator, *Iranian J. Pharm. Res. Int: IJPR*, 15 (2016) 107.
- [26] R. Seifie-Makrani, N. Sajjadi, O. Younesi, H. Bagheri, A new strategy for determination of captopril as a hypertension drug using zno nanoparticle modified carbon paste electrode, *Int. J. Electrochem. Sci.*, 9 (2014) 1799-1811.
- [27] H. Karimi-Maleh, M.R. Ganjali, P. Norouzi, A. Bananezhad, Amplified nanostructure electrochemical sensor for simultaneous determination of captopril, acetaminophen, tyrosine and hydrochlorothiazide, *Mater. Sci. Eng. C*, 73 (2017) 472-477.
- [28] H. Karimi-Maleh, K. Ahanjan, M. Taghavi, M. Ghaemy, A novel voltammetric sensor employing zinc oxide nanoparticles and a new ferrocene-derivative modified carbon paste electrode for determination of captopril in drug samples, *Anal. Methods*, 8 (2016) 1780-1788.
- [29] D.M. da Silva, M.C. da Cunha Areias, Rutin as an electrochemical mediator in the determination of captopril using a graphite paste electrode, *Electroanalysis*, 32 (2020) 301-307.
- [30] M. Shahbakhsh, Z. Hashemzaei, S. Narouie, Y. Shahbakhsh, M. Noroozifar, Gold Nanoparticles/Biphenol-biphenolquinone for Ultra-trace Voltammetric Determination of Captopril, *Electroanalysis*, 33 (2021) 713-722.

COPYRIGHTS



© 2022 by the authors. Licensee PNU, Tehran, Iran. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution 4.0 International (CC BY4.0) (<http://creativecommons.org/licenses/by/4.0>)

یک حسگر پتانسیومتری جدید برای اندازه‌گیری سریع کاپتوپریل در فرمولاسیون دارویی و نمونه‌های بیولوژیکی

پروین پورحکاک^۱، محمدعلی کریمی^{۱*}، حسین توللی^۱، پوران پورحکاک^۱،

محمد مظلوم اردکانی^۲

۱. گروه شیمی، دانشگاه پیام نور، تهران، ایران

۲. گروه شیمی، دانشکده علوم، دانشگاه یزد، یزد، ایران

تاریخ دریافت: ۳ اردیبهشت ۱۴۰۱ تاریخ پذیرش: ۲۰ تیر ۱۴۰۱

چکیده

یک حسگر پتانسیومتری جدید بر اساس یک الکتروود خمیر کربن (CPE) اصلاح‌شده β -سیکلودکسترین برای اندازه‌گیری داروی کاپتوپریل طراحی شده است. اثر β -سیکلودکسترین‌های مختلف (سیکلودکسترین‌های α ، β و γ) و درصد آن‌ها، عامل چسبنده و افزودنی یونی بر پاسخ پتانسیل بررسی شده و الکتروودی با بهترین پاسخ پتانسیل بدست آمد. محدوده غلظت خطی برای این الکتروود 1.0×10^{-7} تا 7.0×10^{-5} مولار با حد تشخیص پایین 2.0×10^{-7} مولار بود. تأثیر pH و دما بر شیب نرنستی نیز بررسی شد و محدوده بهینه بدست آمد. گزینش پذیری CPE captopril به گونه‌های مزاحم شامل Li^+ ، K^+ ، Ni^{2+} ، Mg^{2+} ، Ca^{2+} ، Co^{2+} ، Cr^{2+} ، Cr^{3+} ، Zn^{2+} ، Mn^{2+} ، Fe^{2+} ، Cl^- ، SO_4^{2-} ، PO_4^{3-} ، $C_2O_4^{2-}$ ، $C_2O_4^{2-}$ ، آسکوربیک اسید، اوریک اسید، گلوکز، D- فروکتوز و ساکارز با روش محلول جداگانه (SSM) و روش پتانسیل همسان (MPM) تعیین شد. در نهایت، الکتروود پیشنهادی برای اندازه‌گیری کاپتوپریل در فرمولاسیون دارو، سرم خون و نمونه‌های ادرار مورد آزمایش قرار گرفت.

واژه‌های کلیدی

حسگر پتانسیومتری، کاپتوپریل، β -سیکلودکسترین، الکتروود خمیر کربن اصلاح‌شده، الکتروود انتخابگر یونی.