

*Full Paper*

## **A Novel Electrochemical Nanosensor for Voltammetric Determination of Isoproterenol**

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**Abstract-** A new isoproterenol electrochemical nano sensor was fabricated using a acarbon paste electrode modified with ionic liquid (n-hexyl-3-methylimidazolium hexafluoro phosphate) and magnetic core-shell nanoparticles (MCSILCPE). The electrochemical study of the modified electrode, as well as its efficiency for oxidation of isoproterenol, is described. Differential pulse voltammetry (DPV) exhibits a linear dynamic range from  $1.0 \times 10^{-6}$  to  $7.0 \times 10^{-4}$  M isoproterenol. The limit of detection was equal to  $6.3 \times 10^{-7}$  M. The electrode was also employed to determination of isoproterenol in real samples.

**Keywords-** Isoproterenol, Magnetic core-shell nanoparticles, Ionic liquids, Drug analysis

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### **1. INTRODUCTION**

Electroanalytical methods have been proven to be rapid, simple and sensitive and have an impact in the most of fields of science, for example clinical diagnostics, food quality control, security and environmental analysis. Chemically modified electrodes (CMEs) offer important advantages for electrochemical reactions such as; minor over potentials, higher reaction rates, extra sensitivity and improved selectivity [1-15].

Advances in nanotechnology offer new directions in the design and development of electronic devices including field-effect transistors, detectors and light-emitting diodes, sensors, catalyst supports, solar cells, lithium ion batteries, environmental monitoring, and so on [16-19]. Nanomaterials have received intensive research interest in recent decades due to their unique structure-dependent properties and potential applications in numerous fundamental and applied fields [20-26]. Because of their unique physical and chemical properties such as small dimensional size, good stability, biocompatibility, good conductivity and excellent catalytic activity, nanomaterials have potential applications in the construction of electrochemical sensors and biosensors [27-36].

Recently room temperature ionic liquid (RTIL) has been used as a new kind of modifier for a chemically modified electrode. RTIL is composed entirely of ions and exists as a liquid at room temperature with the characteristics of negligible vapor pressure and good solubility and chemical stability. As a new green media, RTIL has many unique electrochemical properties, such as higher ionic conductivity and wider electrochemical windows [37-44].

Drug analysis plays important roles in drug quality control, and has a great impact on public health. Therefore, a simple, sensitive and accurate method for the determination of active ingredient is very important.

Isoproterenol or 4-[1-hydroxy-2-[(1-methylethyl)- amino] ethyl]-1, 2-benzenediol is a catecholamine drug widely used for hypertension and allergic emergencies, bronchitis, cardiac shock and heart attack. Isoproterenol has positive inotropic and chronotropic effects on the heart and is used for bradycardia or heart block, but overdose of the drug may cause heart failure and arrhythmias [45]. Isoproterenol is readily absorbed when given parenterally or as an aerosol. Absorption of sublingual or oral doses is unreliable. The drug is poorly absorbed from stomach, but well absorbed from small intestine, proximal colon, rectum and from the mucous membrane of the trachea. It is recognized that the dosage requirements for isoproterenol vary widely according to the route of administration; when the drug is given intravenously pharmacological effects are seen with only few micrograms (16-17), whereas using the oral route, tablets containing 180–360mg are required daily to control chronic heart block [46]. The chemically modified electrodes have been widely used as sensitive and favorable analytical methods for determination of Isoproterenol [47-50].

In the present work, we describe the preparation of a new carbon paste electrode modified with an ionic liquid and magnetic core-shell manganese ferrite nanoparticles (MCSILCPE) and investigate its performance for the determination of isoproterenol.

## 2. EXPERIMENTAL

### 2.1. Apparatus and chemicals

The electrochemical measurements were performed with an Autolab potentiostat/galvanostat (PGSTAT 302N, Eco Chemie, the Netherlands). The experimental conditions were controlled with General Purpose Electrochemical System (GPES) software. A conventional three electrode cell was used at  $25 \pm 1$  °C. An Ag/AgCl/KCl (3.0 M) electrode, a platinum wire, and MCSILCPE were used as the reference, auxiliary and working electrodes, respectively. A Metrohm 710 pH meter was used for pH measurements.

Isoproterenol and all of the other reagents were of analytical grade and were obtained from Merck (Darmstadt, Germany). The buffer solutions were prepared from orthophosphoric acid and its salts in the pH range of 2.0-9.0. Ionic liquid (n-hexyl-3-methylimidazolium hexafluoro phosphate) was purchased from Sigma Aldrich Co. magnetic core-shell manganese ferrite nanoparticles were synthesized in our laboratory as reported previously [51].

### 2.2. Preparation of the electrode

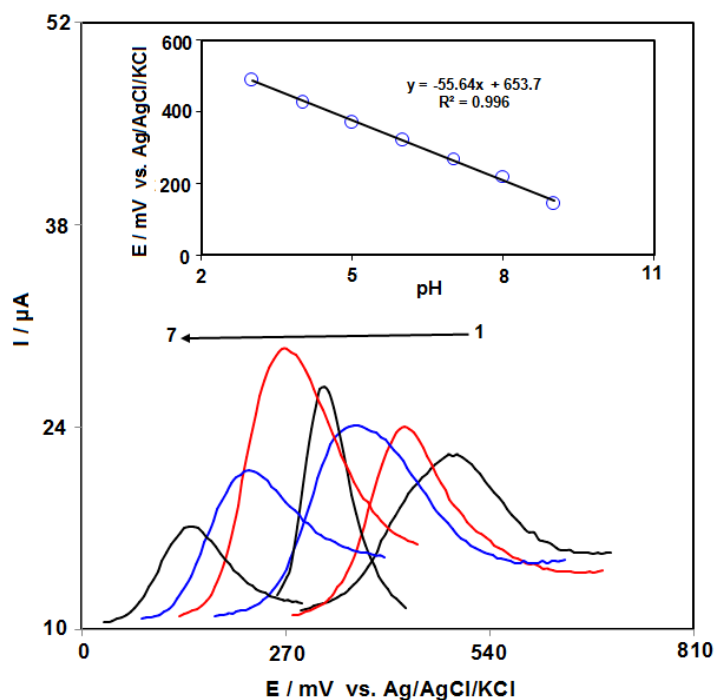
MCSILCPEs were prepared by mixing 0.04 g of magnetic core-shell manganese ferrite nanoparticles with 0.96 g graphite powder and approximately, ~0.8 mL of ionic liquids with a mortar and pestle. The paste was then packed into the end of a glass tube (ca. 3.4 mm i.d. and 15 cm long). A copper wire inserted into the carbon paste provided the electrical contact.

For comparison, ionic liquid / carbon paste electrode in the absence of magnetic core-shell manganese ferrite nanoparticles (ILCPE), magnetic core-shell manganese ferrite nanoparticles carbon paste electrode (MCSCPE) consistent of magnetic core-shell manganese ferrite nanoparticles, graphite powder and paraffin oil, and bare carbon paste electrode (CPE) consisting of graphite powder and paraffin oil were also prepared in the same way.

## 3. RESULT AND DISCUSSION

### 3.1. Influence of pH

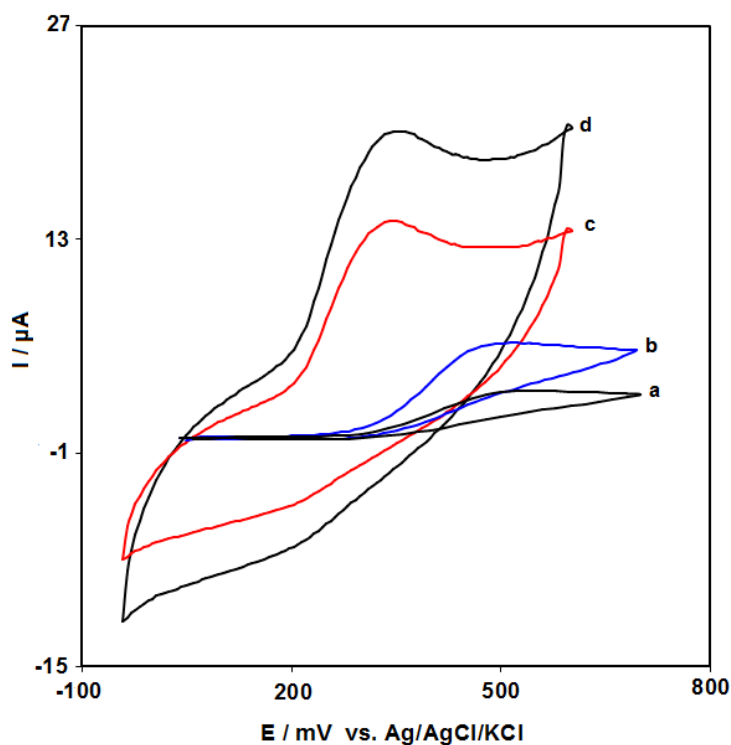
The electrochemistry of isoproterenol is generally pH dependent. Thus, the electrochemical behavior of isoproterenol was studied at different pHs using DPV (Fig. 1). It was noticeable that the anodic peak potentials of the isoproterenol shift to less positive values with increasing pH. The inset of Fig. 1 shows potential–pH diagrams constructed by plotting the peak potential values as functions of pH. As can be seen, the slope is 55.64 mV/pH indicating that the system obeys the Nernst equation for an equal electron and proton transfer reaction [52].



**Fig. 1.** DPVs (at  $50 \text{ mV s}^{-1}$ ) of the MCSILCPE in the presence of  $200.0 \text{ } \mu\text{M}$  isoproterenol at various buffered pHs. The numbers 1–7 correspond to pHs 3.0, 4.0, 5.0, 6.0, 7.0, 8.0 and 9.0, respectively. Inset: plot of  $E_p$  vs. pH

### 3.2. Electrochemical behavior of isoproterenol at the surface of various electrodes

Fig. 2 displays cyclic voltammetric responses from the electrochemical oxidation of  $125.0 \text{ } \mu\text{M}$  isoproterenol at the surface of MCSILCPE (curve d), ILCPE (curve c), MCSCPE (curve b) and bare CPE (curve a). The results showed that the oxidation of isoproterenol is very weak at the surface of the bare CPE, but in the presence of ILs in CPE could enhance the peak current and decrease the oxidation potential (decreasing the overpotential). A substantial negative shift of the currents starting from oxidation potential for isoproterenol and dramatic increase of the current indicates the catalytic ability of MCSILCPE (curve d) and ILCPE (curve c) to isoproterenol oxidation. The results showed that the combination of magnetic core-shell manganese ferrite nanoparticles and the ionic liquid (curve d) definitely improved the characteristics of isoproterenol oxidation. However, MCSILCPE shows much higher anodic peak current for the oxidation of isoproterenol compared to ILCPE, indicating that the combination of magnetic core-shell manganese ferrite nanoparticles and IL has significantly improved the performance of the electrode toward isoproterenol oxidation.

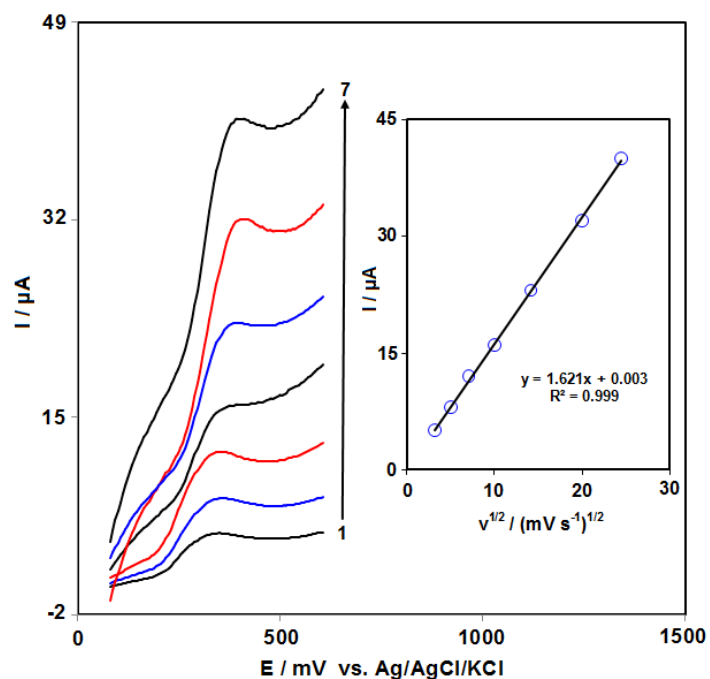


**Fig. 2.** CVs of a) CPE, b) MCSCPE, c) ILCPE and d) MCSILCPE in the presence of 125.0  $\mu\text{M}$  isoproterenol at a pH 7.0, respectively. In all cases the scan rate was  $50 \text{ mV s}^{-1}$

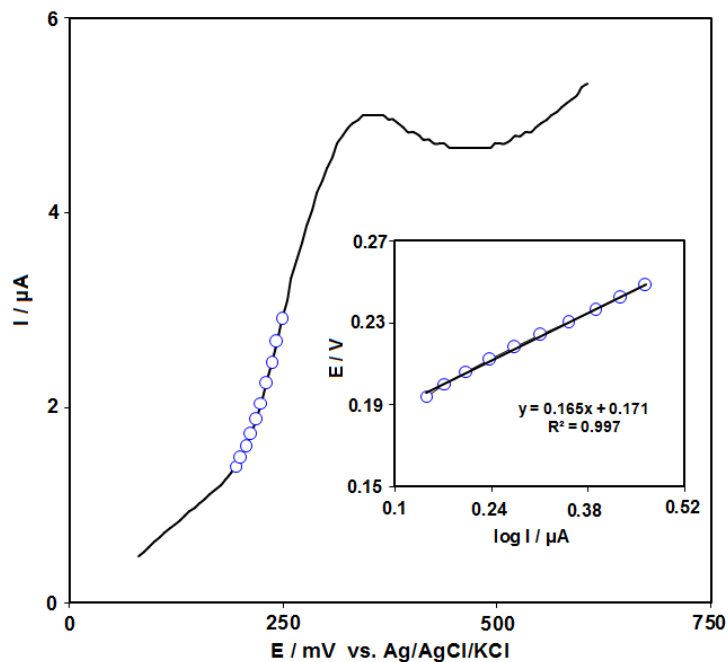
### 3.3. Effect of scan rate

The effect of potential scan rates on the oxidation current of isoproterenol has been studied (Fig. 3). The results showed that increasing in the potential scan rate induced an increase in the peak current. In addition, the oxidation process is diffusion controlled as deduced from the linear dependence of the anodic peak current ( $I_p$ ) on the square root of the potential scan rate ( $v^{1/2}$ ) over a wide range from 10 to  $600 \text{ mVs}^{-1}$ .

Fig. 3 shows the LSV of MCSILCPE obtained in 0.1 M PBS (pH 7.0) containing  $50.0 \mu\text{M}$  isoproterenol, with a sweep rate of  $10 \text{ mVs}^{-1}$ . The points show the rising part of the voltammograms (known as the Tafel region), which is affected by the electron transfer kinetics between isoproterenol and MCSILCPE. If deprotonation of isoproterenol is a sufficiently fast step, the number of electrons involved in the rate determining step can be estimated from the slope of the Tafel plot. The inset of Fig. 4 shows a Tafel plot that was drawn from points of the Tafel region of the LSV. The Tafel slope of 0.165 V obtained in this case agrees well with the involvement of one electron in the rate determining step of the electrode process, assuming a charge transfer coefficient of  $\alpha=0.64$ .



**Fig. 3.** LSVs of MCSILCPE in 0.1 M PBS (pH 7.0) containing 50.0  $\mu\text{M}$  isoproterenol at various scan rates; numbers 1-7 correspond to 10, 25, 50, 100, 200, 400 and 600  $\text{mV s}^{-1}$ , respectively. Inset: Variation of anodic peak current vs. square root of scan rate



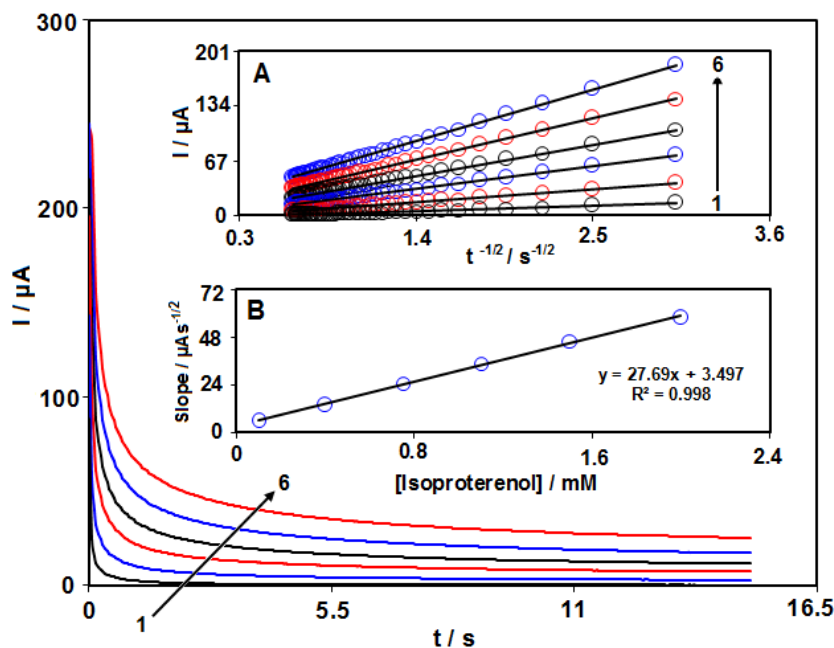
**Fig. 4.** LSV (at  $10 \text{ mVs}^{-1}$ ) of a MCSILCPE in 0.1 M PBS (pH 7.0) containing 50.0  $\mu\text{M}$  isoproterenol. The points are the data used in the Tafel plot. The inset shows the Tafel plot derived from the LSV

### 3.4. Chronoamperometric measurements

Chronoamperometric measurements of isoproterenol at MCSILCPE were carried out by setting the working electrode potential at 0.4 V vs. Ag/AgCl/KCl (3.0 M) for the various concentrations of isoproterenol in PBS (pH 7.0) (Fig. 5). For an electroactive material (isoproterenol in this case) with a diffusion coefficient of  $D$ , the current observed for the electrochemical reaction at the mass transport limited condition is described by the Cottrell equation [52].

$$I = nFAD^{1/2}C_b\pi^{-1/2}t^{-1/2} \quad (1)$$

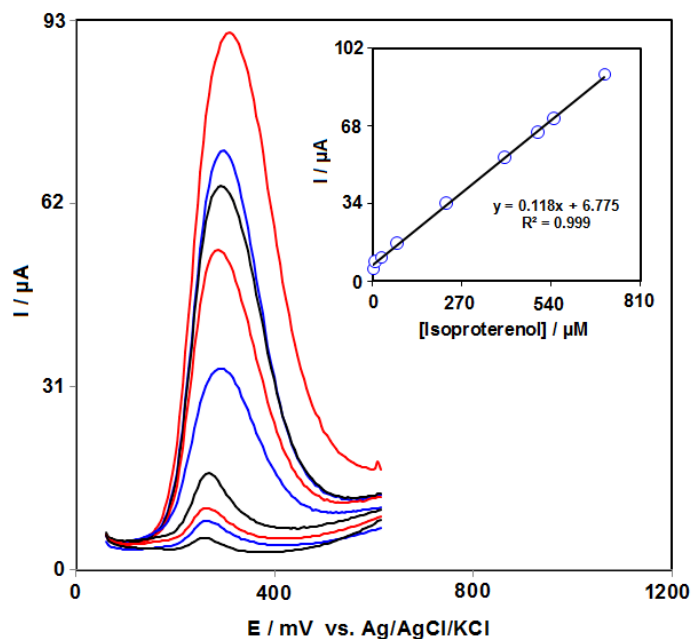
Where  $D$  and  $C_b$  are the diffusion coefficient ( $\text{cm}^2 \text{s}^{-1}$ ) and the bulk concentration ( $\text{mol cm}^{-3}$ ), respectively. Experimental plots of  $I$  vs.  $t^{-1/2}$  were employed, with the best fits for different concentrations of isoproterenol (Fig. 5A). The slopes of the resulting straight lines were then plotted vs. isoproterenol concentration (Fig. 5B). From the resulting slope and Cottrell equation the mean value of the  $D$  was found to be  $7.96 \times 10^{-6} \text{ cm}^2/\text{s}$ .



**Fig. 5.** Chronoamperograms obtained at MCSILCPE in 0.1 M PBS (pH 7.0) for different concentration of isoproterenol. The numbers 1–6 correspond to 0.1, 0.4, 0.75, 1.1, 1.5 and 2.0 mM of isoproterenol. Insets: (A) Plots of  $I$  vs.  $t^{-1/2}$  obtained from chronoamperograms 1–6. (B) Plot of the slope of the straight lines against isoproterenol concentration.

### 3.5. Calibration plot and limit of detection

The peak current of isoproterenol oxidation at the surface of the modified electrode can be used for determination of isoproterenol in solution. Therefore, DPV experiments were done for different concentrations of isoproterenol (Fig. 6). The oxidation peak currents of isoproterenol at the surface of a modified electrode were proportional to the concentration of the isoproterenol within the ranges  $1.0 \times 10^{-6}$  to  $7.0 \times 10^{-4}$  M with detection limit ( $3\sigma$ ) of  $6.3 \times 10^{-7}$  M.



**Fig. 6.** SWVs of MCSILCPE in 0.1 M PBS (pH 7.0) containing different concentrations of isoproterenol (1.0, 10.0, 25.0, 75.0, 225.0, 400.0, 500.0, 550.0 and 700.0  $\mu\text{M}$ ). Inset shows the plots of the peak current as a function of isoproterenol concentration in the range of 1.0-700.0  $\mu\text{M}$

### 3.6. Real sample analysis

In order to evaluate the analytical applicability of the proposed method, also it was applied to the determination of isoproterenol in isoproterenol ampoule and urine samples. The results for determination of the isoproterenol in urine sample are given in Table 1. Satisfactory recovery of the experimental results was found for isoproterenol. The reproducibility of the method was demonstrated by the mean relative standard deviation (R.S.D.).



**Table 1** The application of MCSILCPE for determination of isoproterenol in real samples (n=5)

Sample	Spiked	Found	Recovery (%)	R.S.D. (%)
Hydrochlorothiazide Ampoule	0	10.0	-	3.4
	5.0	15.2	101.3	2.1
	10.0	19.4	97.0	1.9
	15.0	25.9	103.9	2.9
	20.0	29.8	99.3	2.6
Urine	0	-	-	-
	7.5	7.7	102.7	2.3
	12.5	12.4	99.2	3.2
	17.5	17.7	101.1	1.8
	22.5	22.1	98.2	2.4

#### 4. CONCLUSION

A ncarbon paste electrode was modified with nanoparticles and ionic liquid. Then it was applied to voltammetric determination of isoproterenol in aqueous buffer solutions. Finally it was applied to determination of isoproterenol in isoproterenol ampoule and urine samples. The proposed modified electrode presented a low detection limit and good linear range and reproducibility which make it a suitable isoproterenol sensor for practical applications.

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