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Synthesis of N-isopropylphenoxypropanolamine analogue and their electrocatalysis for the determination of dopamine: A cyclic voltammetric study

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ABSTRACT

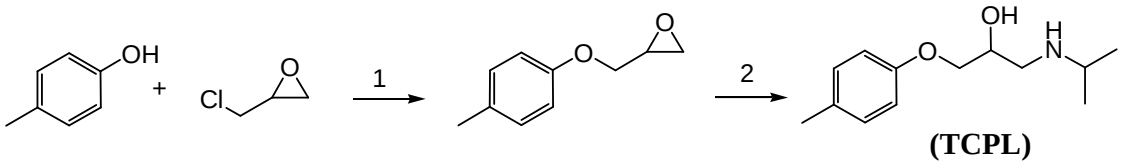
1-(p-tolyloxy)-3-chloropropan-2-ol (TCPL) was prepared as an analogue to the N-isopropylphenoxypropanolamine and it was characterized by LCMS, ^{1}H NMR and purity by HPLC. The prepared compound was used as a modifier for the electrochemical determination of dopamine (DA). The effect of scan rate, concentration and pH was studied. The overall electrode process was found to be both adsorption and diffusion controlled. The effect of concentration and pH was studied. The detection limit of DA at the modified electrode was found to be 4.5 X 10 $^{-7}$ M. Hence this electrode can be used for the selective and sensitive determination of DA.

Keywords: TCPL, carbon paste electrode, dopamine, electrochemical oxidation, cyclic voltammetry.

INTRODUCTION

Dopamine (DA) is one of the most significant, catecholamine belonging to the family of excitatory chemical neurotransmitter [1, 2]. It plays very important role in the function of central nervous, renal, hormonal and cardio vascular system [3-4]. Because extreme abnormalities of DA level are symptoms of several diseases such as schizophrenia, Parkinson's disease [5], the determination of such compounds in a real biological sample and identify changes in neurotransmission that correlate the behavioral state of animal are an obvious target in neurochemical studies. Generally the determination of DA is performed with high performances liquid chromatography (HPLC) [6], ion chromatography [7] and spectrophotometry. DA can be determined by electrochemical methods because it is an electrochemical compound. DA can be determined by electrochemical methods because it is an electrochemical compound. The development of voltammetric sensor for the detection of neurotransmitter in the extracellular

fluid of the central nervous system has received much interest in the past few decades [8-9]. The electrochemical methods have more advantages over other methods because the electrodes can be made conveniently to sense the neurotransmitter in the living organism [10]. A number of modified carbon electrode was developed for the determination of DA by using voltammetric techniques [11]. Modification can be done by grinding in an agate mortar [12-14], by electropolymerisation [15-16] and also by immobilization method [17]. Modified carbon paste electrode can be prepared by adding different types of modifiers such as chemicals, enzymes etc. In a search of a chemical modifier we found losartan [12] shown good sensitivity towards the determination of DA. In this contest for this work further synthesized N-isopropylphenoxypropanolamine analogue i.e. 1-(p-tolyloxy)-3-chloropropan-2-ol (TCPL) and studied their electrochemical behavior with modification. The compound TCPL was synthesized as per the Scheme-1[18, 19] and used for the determination of electrochemical response of DA.



(TCPL)

Reagents;(1) Piperidine,Reflux 6hrs. (2) Isopropyl amine, Methanol,Reflux 4hrs.

Scheme.1-Synthesis and Structure of 1-(p-tolyloxy)-3-chloropropan-2-ol (TCPL)

The aim of the work was to establish a simple and sensitive electrochemical method for the determination of dopamine in the presence of TCPLMCPE. The oxidation peak current of dopamine remarkably increases at the CPE suggesting significant improvement of determining sensitivity. Thus the present study provides a method for selective and sensitive detection of DA, which has a significant attraction in biological and chemical fields.

MATERIALS AND METHODS

2.1. Reagents and Chemicals

4-Cresol, Epichlorohydrin, Piperidine and Dopamine hydrochloride were purchased from Himedia. Grahite powder (50 micrometer particle size) was purchased from Lobo Chemie and silicon oil was purchased from HIMEDIA. DA stock solution was prepared in 0.1 M perchloric acid ($HClO_4$) solution. The phosphate buffer solution (0.2 M) was prepared using the appropriate mixtures of disodium hydrogen phosphate and sodium dihydrogen phosphate and used as supporting electrolyte in the investigation of DA. Chemicals mentioned above were all purchased from Fluka, were analytical grade and used without purification.

2.2. Apparatus

NMR spectra were recorded on a Bruker-400 MHz spectrometer and are expressed in ppm using TMS as internal reference. Mass spectra were recorded on a Finnigan 4000 series GC/MS Mass spectrometer. The electrochemical experiments were carried out using a Model-201 Electroanalyser [EA-201 Chemilink system]. All the experiments were carried out in a convectional three electrochemical cell. The electrode system contained a working carbon paste electrode (home made cavity of 3mm diameter), a platinum wire as counter electrode and saturated calomel electrode as reference electrode.

2.3. Synthesis of 1-(p-tolyloxy)-3-chloropropan-2-ol (TCPL)

1-(p-tolyloxy)-3-chloropropan-2-ol was prepared by condensing with p-Cresol with excess epichlorohydrin in a presence of piperidine and it was further reacted with isopropyl amine and methanol at reflux temperature for 4 h to produce the desired compound. The synthesized product was characterized by NMR and Mass Spectra. m.p. 92-94°C, LC-MS: m/z 224 [M+]; ^{1}H NMR(DMSO-d_6) : δ 1.0 (6H, s,-CH3), δ 1.5 (1H, -NCH), δ 2.2(3H,s,Ar-CH3), δ 2.5 (1H,m, -NCH)), δ2.6 (2H, m,NCH2-), δ 3.81 (1H,m,CHOH),δ 3.9(2H,m,Ar-OCH-): δ 4.9 (1H, s ,-OH), δ 6.7 (2H, d, Ar-CH), δ 7.0 (2H, d, Ar-CH).

2.4. Preparation of carbon paste electrode

The carbon paste electrode was prepared by hand mixing 70% graphite powder and 30% silicon oil by hand mixing in an agate mortar for about 30min to get homogeneous carbon paste. This carbon paste was then packed into the cavity of a Teflon tube electrode (3mm in diameter). Before the measurement modified electrode was smoothed on a piece of transparent paper to get a uniform, smooth and fresh surface.

RESULTS AND DISCUSSION

3.1 Effect of TCPL as Modifier for investigation of DA (TCPLMCPE)

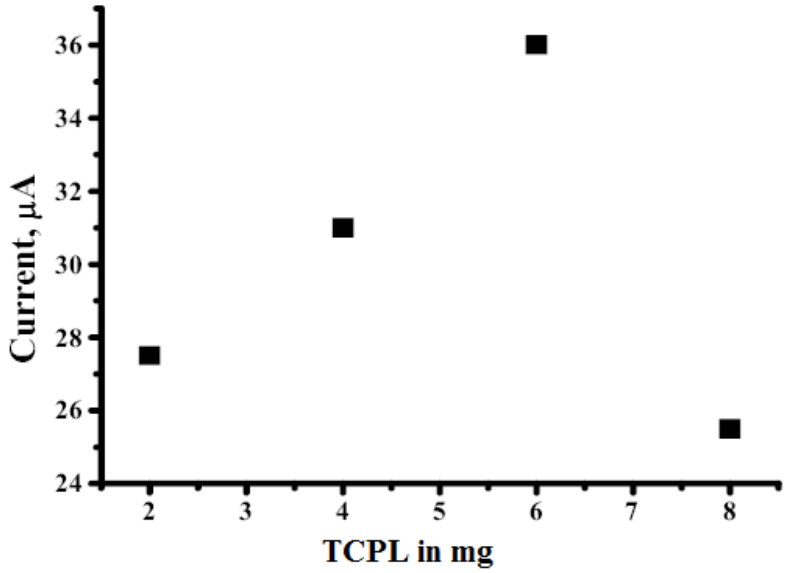


Figure.1-Graph of Ipa of DA vs different quantity of TCPL in carbon paste electrode.

TCPLMCPE was prepared of different ratio by adding different amount of TCPL By increasing the quantity of TCPL in the modification, the electrochemical cathodic and anodic peak currents (Ipa) goes on increasing at certain ratio. The modification of TCPLMCPE from 2mg to 8mg has calibrated and the redox peak currents were increased up to 6 mg TCPL in carbon paste electrode. Above 6 mg of TCPL the redox peak currents was decreased (Fig.1). Further increase in the quantity of TCPL both Ipa and Ipc were decreased. Therefore 6 mg TCPL was taken as constant for the preparation of TCPLMCPE.

3.2 The electrochemical response of Dopamine at TCPLMCPE

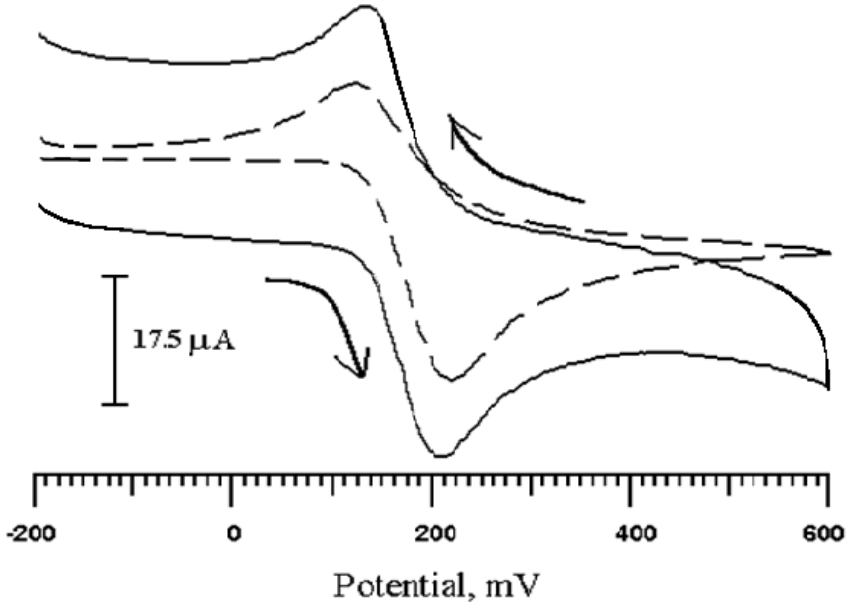


Figure.2-Cyclic voltammogram of 1mM DA in 0.2M phosphate buffer solution at pH 7 at BCPE (dotted line) and TCPLMCPE (solid line), at 50 mVs^{-1} in 0.2M phosphate buffer solution (pH. 7.2).

Fig.2. shows the cyclic voltammograms obtained for the electrochemical response of DA at TCPLMCPE (solid line curve) and bare carbon paste electrode (dashed line curve) in 0.2 M phosphate buffer solution pH 7.2 containing 1 mM DA scan rate 50 mV/s. At bare CPE, the oxidation and reduction peak potentials of DA occurs at 218 and 121 mV respectively. Under the identical conditions, TCPLMCPE produces increased peak currents of DA with the oxidation and reduction peak potentials at 214 and 134 mV respectively. The ΔEp was found to be 80 mV. The enhancement in redox peak currents suggested the electrochemical property of TCPLMCPE towards the DA detection.

3.3 Effect of Scan Rate

According to Randles-Sevick's equation, current is proportional to scan rate. The TCPLMCPE showed increase in the peak current with increase in scan rate (50 to 300mV/s) in 1mM dopamine in 0.2M phosphate buffer solution at pH 7.0. Cyclic voltammogram for dopamine at TCPLMCPE was shown in Fig.3a. The graph of anodic peak current Ipa vs. scan rate (υ) and square root of scan rate ($\upsilon^{1/2}$) were plotted as shown in Fig.3b.and Fig.3c respectively. The graphs obtained in the range from 50 to 300 mV/s the anodic peak current was proportional to the scan rate (υ) and also the square root of scan rate ($\upsilon^{1/2}$) with correlation coefficient 0.9938 and 0.9984 respectively. This indicates that, the electrode transfer reaction was both adsorption and diffusion controlled [20].

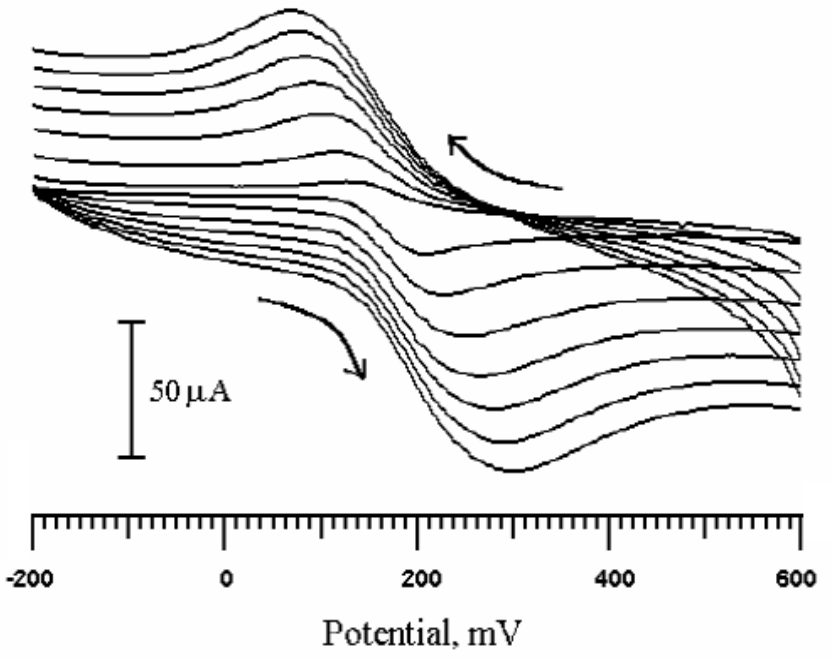


Figure.3a-Cyclic voltammogram of 1mM DA at different scan rate (50 to 300 mVs^{-1}) at TCPLMCPE in 0.2M phosphate buffer solution (pH 7.2).

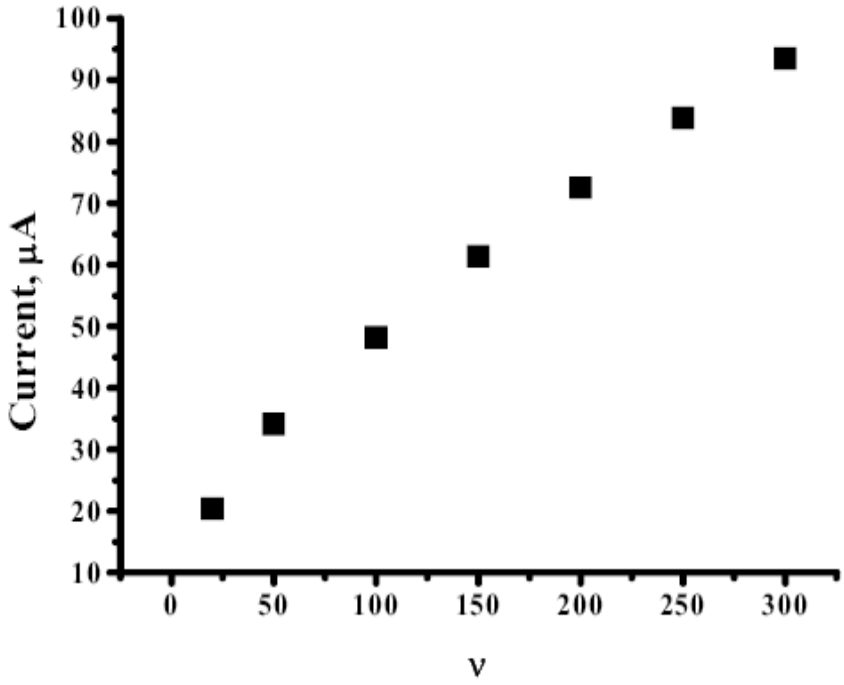


Figure.3b-Graph of current vs scan rate of DA.

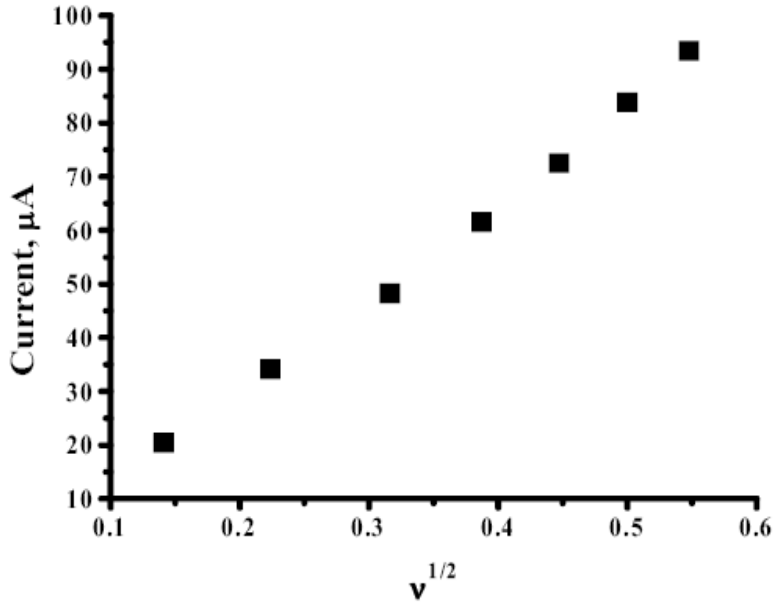


Figure.3c-Graph of current vs square root of scan rate of DA.

3.4 Effect of DA concentration

The electrocatalytic oxidation of DA was carried out by varying the concentration at TCPLMCPE. By increasing the concentration of DA from 1 mM DA to 5mM DA, the Ipa and Ipc goes on increasing with shifting of Epa and Epc. The graph of Ipa vs concentration of DA was plotted and it showed increase in anodic peak current.(Fig. 4). The graph obtained linearly increases in peak current with increase in the DA concentration. This indicates the process is adsorption controlled [21, 22].

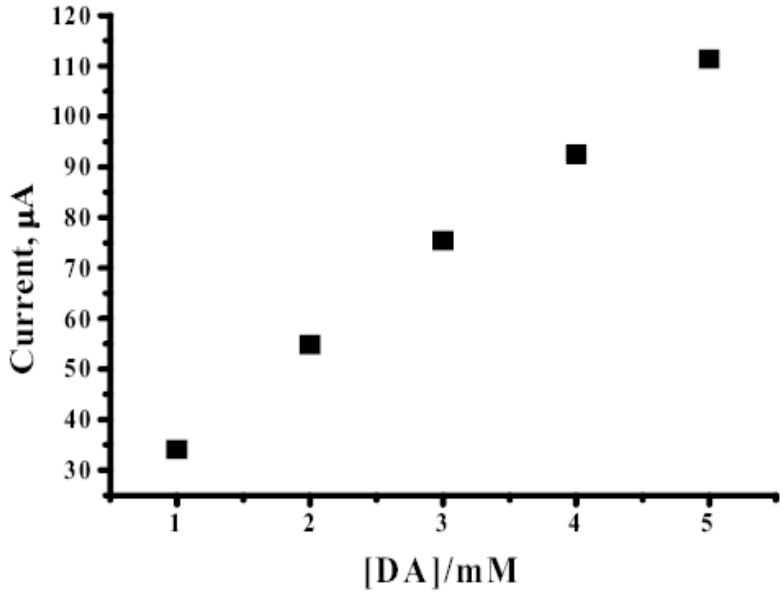


Figure.4-Graph of current vs concentration of DA.

3.5 Effect of pH

The effect of variation of pH was studied for 1mM DA in the range from 2.0 to 9.0 using 0.2M phosphate buffer as a supporting electrolyte at scan rate of 50mV/s at TCPLMCPE. The electrochemical response of DA at TCPLMCPE is generally *p*H dependent. Both anodic and cathodic peak potentials were shifted to less positive side with increasing in the pH values. The anodic peak potential of DA shifted from 330 mV to 170 mV with respect to the *p*H from 2 to 9. The potential diagram was constructed by plotting the graph of calculated E^0 vs *p*H of the solution (fig. 5). The graph has good linearity with a slope of 50 mV/*p*H, this behavior is nearly obeyed the Nernst Equation for two electrons and two proton transfer reaction [21, 23].

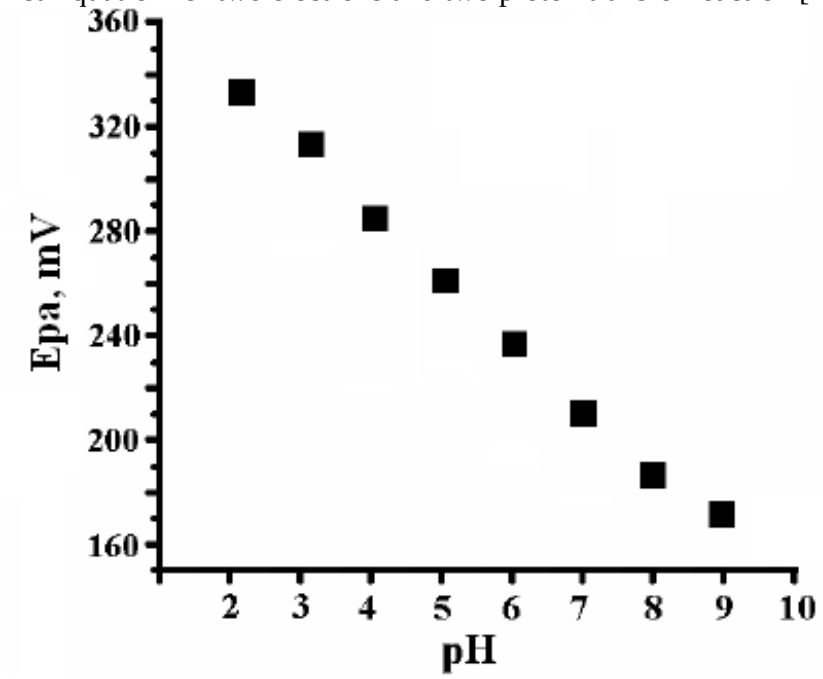


Figure.5-Graph of E^0vs *p*H

CONCLUSION

The electrochemical behavior of DA was studied at carbon paste electrode by cyclic voltammetry. The TCPL modified carbon paste electrode has shown high sensitivity for voltammetric peaks of dopamine. The high sensitivity, easy preparation, surface regeneration of the modified electrode and the reproducibility of the voltammetric response make the prepared modified system very useful in the construction of simple devices for the determination of dopamine in clinical and pharmaceutical preparations.

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