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Research Article

Electrochemical Investigation of Dicyclomine Hydrochloride at Poly (Terbutaline Sulphate) Modified Carbon Paste Electrode

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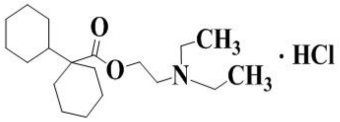
Abstract

Dicyclomine Hydrochloride (DICY) has been studied on electropolymerisation of Terbutaline Sulphate (TBS) modified carbon paste electrode by cyclic voltammetry (CV) and differential pulse voltammetry (DPV). Voltammetric behavior of Dicyclomine Hydrochloride (DICY) on the poly (Terbutaline Sulphate) modified carbon paste electrode was investigated with electrochemical parameters of cyclic voltammetry. The variation of pH, Scan rate, Concentration of Dicyclomine Hydrochloride (DICY) has been studied. In optimal conditions, the oxidation peak current of DICY on the poly (Terbutaline Sulphate) modified carbon paste electrode was enhanced greatly indicating high sensitivity. The low detection limit (LOD) and low detection quantity (LOQ) of DICY has been found to be 0.12 µM and 0.408 µM with a correlation coefficient of 0.99461. The practical application of the modified electrode in the determination of DICY has good selectivity and high sensitivity.

Keywords: Terbutaline Sulphate, Dicyclomine Hydrochloride, Electropolymerization, Carbon Paste Electrode, Cyclic Voltammetry, Differential pulse voltammetry

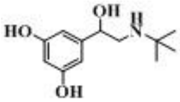
1.Introduction

Dicyclomine Hydrochloride (DICY) chemically is 2-(diethyl amino) ethyl 1 cyclohexylcyclohexane-1-carboxylate (**Scheme I**), is a muscarinic antagonist used as an anti spasmodic and in urinary incontinence. This dual mode of action provides a specific anti cholinergic effect at Acetylcholine receptor and a direct effect upon smooth muscle, but rarely causes any side effect[1].



Scheme I: Dicyclomine Hydrochloride (DICY)

Terbutaline sulfate (TBS), β-[(tert-butylamino) methyl]- 3,5-dihydroxy-benzyl alcohol ($C_{12}H_{19}NO_3$) (**Scheme II**), is a β2-agonist that is widely used as a bronchodilator in acute and long-term treatment of chronic bronchitis, emphysema and other chronic obstructive pulmonary diseases [2].



Scheme II: Terbutaline Sulphate (TBS)

Electropolymerization was a good approach to immobilize polymers to prepare polymer modified electrodes (PMEs) as adjusting the electrochemical parameters can control film thickness, permeation and charge transport characteristics. Polymer-modified electrodes have many advantages in the detection of analytes because of their selectivity, sensitivity and homogeneity in electrochemical deposition, strong adherence to electrode surface and chemical stability of the film [3]. Selectivity of PMEs as a sensor can be attained by different mechanisms such as size exclusion [4]; ion exchange [5]; hydrophobicity interaction [6]; and electrostatic interaction [7] [8].

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The aim of the work is to establish a simple and sensitive electrochemical method for the determination of Dicyclomine Hydrochloride by Poly (Terbutaline Sulphate) modified CPE. The Oxidation peak current of Dicyclomine Hydrochloride increases at the CPE suggesting significant improvement of determining sensitivity. The proposed work has some obvious advantages including high sensitivity, extreme simplicity, rapid response and low cost.

2. Experimental Section

2.1. Reagents

Terbutaline Sulphate (TBS) and Dicyclomine Hydrochloride (DICY) were purchased from Sigma Aldrich and all other chemicals were of analytical grade. The electropolymerisation of Terbutaline Sulphate was performed in 0.2 M phosphate buffer. The phosphate buffer solution was prepared from KH_2PO_4 and K_2HPO_4 and the pH was adjusted with 0.1 N NaOH solution. The stock solution of the Dicyclomine Hydrochloride (10 mM) was prepared by dissolving it in water. Other chemicals used were of analytical grade except for spectroscopically pure graphite powder. All Solutions were prepared with doubly distilled water. Freshly prepared DICY solution is used prior to measurements.

2.2. Apparatus

Electrochemical measurements were carried out with a model-201 electrochemical analyzer (EA-201 chemlink systems) in a Conventional three-electrode system. The working electrode was carbon paste electrode, having cavity of 3 mm diameter. The Counter electrode was Platinum electrode with a saturated calomel electrode (SCE) as a standard reference electrode completing the circuit.

2.3. Modification procedure

2.3.1. Preparation of bare carbon paste electrode

The Bare Carbon paste electrode was prepared by hand mixing of 70% graphite powder and 30% silicon oil were mixed to produce a homogenous carbon paste which was then packed into the cavity of a homemade carbon paste electrode and smoothed on a weighing paper.

2.3.2. Preparation of the Terbutaline Sulphate polymer film modified carbon paste electrode.

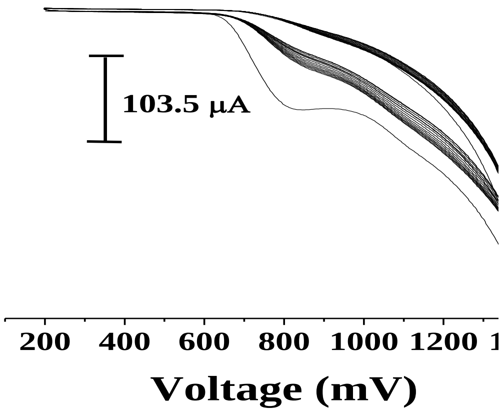
The polymer film modified electrode was prepared by electrochemical polymerization of terbutaline sulphate in 0.2M Phosphate buffer solution (pH 6.0) containing 1 mM Terbutaline sulphate with cyclic voltammetric sweeps in the potential range +200 to +1400 mV at the scan rate 100 mVs^{-1}. After 15 cycles, the surface of the electrode was washed with double distilled water to remove the physically adsorbed material, air dried and used for the electrochemical studies.

3. Result and Discussion

3.1. Electropolymerisation of Terbutaline sulphate on a carbon paste electrode

Electropolymerization of TBS was performed on a CPE. The cyclic voltammograms for the electropolymerisation of 1mM of TBS in 0.2 M Phosphate solution on CPE is shown in **Figure 1** which displays the continuous cyclic voltammetric of 1mM TBS monomer by scanning in the potential range of +200 to +400 mVs^{-1} for 15 cycles. During the electropolymerisation process, indiscernible peaks started to appear after 5th cycle. An anodic peak potential at +861 mV was observed due to the formation of poly (Terbutaline Sulphate). The peak descended gradually with the increase in cyclic time; such decrease indicates the poly (Terbutaline Sulphate) membrane forming and depositing on the surface of the CPE by electropolymerisation. Terbutaline Sulphate was oxidized to free radical at the surface of CPE rapidly resulting in the possible structure of electropolymerised poly (Terbutaline Sulphate). After polymerization the poly (Terbutaline Sulphate) modified CPE was carefully rinsed with distilled water to remove the physically adsorbed material. Then the film electrode was transferred to an electrochemical cell and cyclic voltammetric sweeps were carried out to obtain electrochemical steady state.

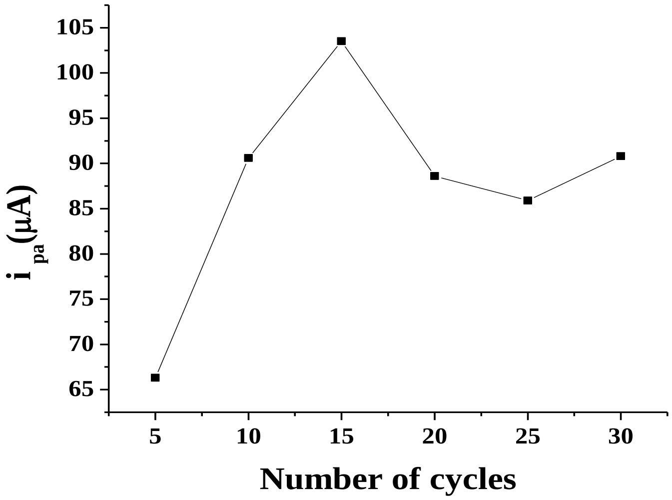
Figure 1: Cyclic voltammograms for the electro polymerization of 1 mM of Terbutaline Sulphate (TBS) in 0.2 M phosphate buffer solution on a CPE.



3.2. Effect of the poly (Terbutaline sulphate) film thickness on the electrochemical response of Dicyclomine Hydrochloride (DICY)

The thickness of poly (Terbutaline sulphate) film could be controlled by the cyclic number of voltammetric scans during the electrochemical modification. The effect of the thickness of poly (Terbutaline Sulphate) film on the electrochemical response was investigated by Cyclic Voltammetric technique. The current (I_{pa}) response of poly (Terbutaline Sulphate) films increase gradually as the number of cycle's increases during film formation from 5 to 15 cycles. Afterwards I_{pa} starts to decrease by increasing the number of cycles which was examined up to 30 cycles **(Figure 1a).** In order to obtain better oxidation peak and higher sensitivity of current for the electrochemical response of Dicyclomine Hydrochloride (DICY). 15 scans were chosen to control the thickness of the poly (Terbutaline Sulphate) film.

Figure 1a: Anodic peak current v/s. Number of cycles of TBS



3.3. SEM Characterization of poly (TBS)-modified carbon paste electrode

Figure 2a and **Figure 2b** explain the surface morphology of bare CPE and poly (TBS) modified CPE respectively using scanning electron microscopy. The surface of bare CPE was formed by irregularly shaped micrometer-sized flakes of graphite. At the modified electrode had atypical uniform arrangement of TBS molecules on the surface of CPE [9].

Figure 2a: SEM images of bare carbon paste electrode.

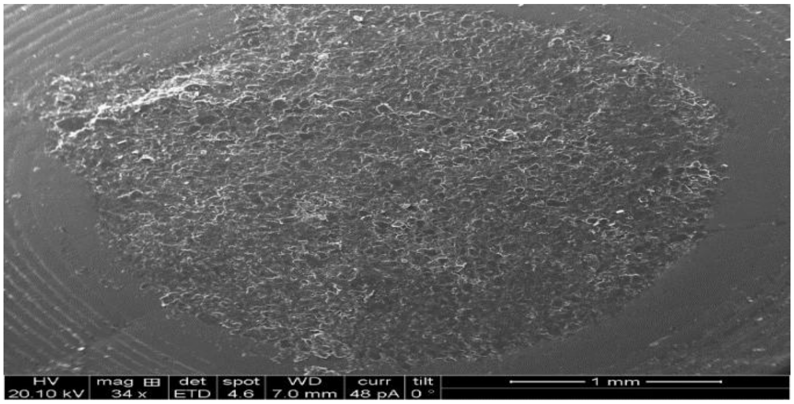
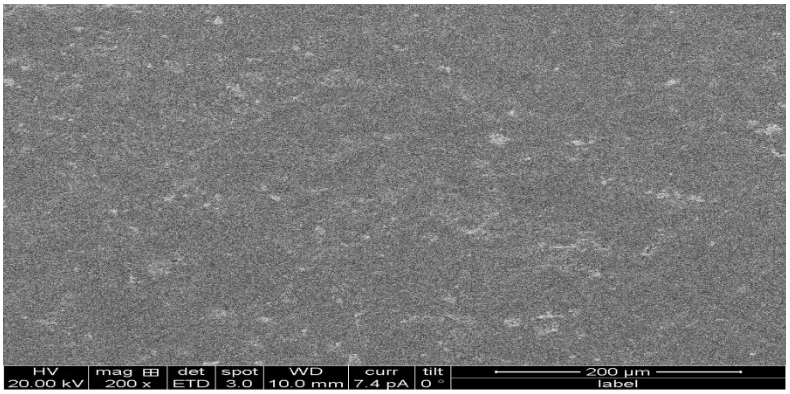


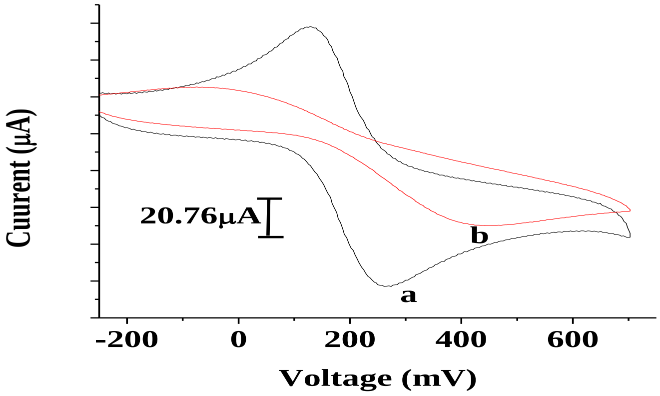
Figure 2b: SEM images of poly (TBS) carbon paste electrode.



3.4. Electrochemical response of potassium ferrocyanide at poly (Terbutaline Sulphate) modified carbon paste electrode

Figure 3. shows the electrochemical response of 1mM potassium ferrocyanide in 1M KCl at bare carbon paste electrode (BCPE) (curve (b) in **Figure 3**) and at poly (Terbutaline Sulphate) modified carbon paste electrode (curve (a) in **Figure 3**).the curve (b) shows the electrochemical response of BCPE having the cathodic peak current (I_{pc}) 6.23 µA and anodic peak current (I_{pa}) 12.48 µA. The electrochemical cathodic peak potential (E_{pc}) 36 mV and anodic peak potential (E_{pa}) 442 mV. After modification with poly (Terbutaline Sulphate) MCPE shows enhancement of both electrochemical anodic peak current (I_{pa}) 20.76 µA and cathodic peak current (I_{pc}) 14.55 µA anodic peak potential (E_{pa}) 262 mV and cathodic peak potential (E_{pc}) 129 mV. The effective area of the modified electrode was found to be 0.0342 cm^2.

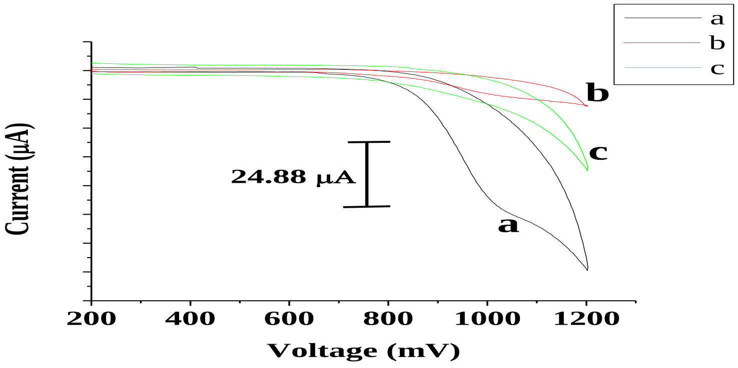
Figure 3: Comparison of 1 mM k_4 [Fe (CN)$_6$] in 1 M KCl solution at poly (TBS) MCPE (a) and BCPE (b).



3.5. Electrochemical behavior of Dicyclomine Hydrochloride at poly (Terbutaline Sulphate) modified CPE

Figure 4 shows cyclic voltammogram of 0.1 mM Dicyclomine Hydrochloride at pH 6.0 in phosphate buffer at bare CPE (curve b) and at poly (Terbutaline Sulphate) modified CPE (curve a) and at blank solution of poly (Terbutaline Sulphate) modified CPE (curve c). Above studies showed that only one oxidation peak at 1030 mV and a anodic peak current of 4.49 µA at bare CPE, whereas an oxidation peak at 992 mV and a anodic peak current of 24.88 µA at the Poly (Terbutaline Sulphate) modified CPE, in the potential range +200 to +1200 mV. No reduction peak was observed in the reverse scan, suggesting that the electrochemical reaction is a totally irreversible process and the oxidation peak at the bare CPE is broad due to slow electron transfer, while the response was considerably improved at the poly (Terbutaline sulphate) modified electrode and the peak potentials shifted to negative direction, the shape of the peak turns sharper and the peak current increased significantly.

Figure 4: Comparision of 0.1 mM DICY at poly (Terbutaline Sulphate) modified CPE (a), Bare CPE (b) and Blank Solution in Phosphate buffer (c), 50 mVs^{-1}.



3.6. Effect of pH

The pH influence was investigated by cyclic voltammetric measurement at different pH values between 2.5 and 9.0 as shown in **Figure 5a**. The maximum response current was observed at pH 6.0. In order to obtain the maximum bioactivity and optimal sensitivity, phosphate buffer of pH 6.0, 50 mVs^{-1} was selected for our experiments. The oxidation peak current increases with increase of pH from 2.5 to 6 and becomes maximum and peak potential shifted negatively. While pH beyond 6, a great decrease of the oxidation peak current could be observed, then it decreased gradually with the further increasing the pH of solution as shown in **Figure 5a** and the oxidation peak potential decrease with increase of pH as shown in **Figure 5b**. A linear relationship was obtained between the anodic peak potential and pH of the solution in the range 2.5 – 9. The linear regression equation was given by:

$$E_{pa}\,(\text{mV}) = 1138.217 - 41.367\ \text{pH} \qquad (R = 0.99386),$$

With a negative slope of 41.367 indicating that the number of electron and proton is equal in the electrochemical oxidation of DICY at Poly (TBS) MCPE.

Figure 5a: Plot of anodic peak current vs. pH (2.5 – 9.0) of 0.1 mM DICY at the poly (TBS) MCPE.

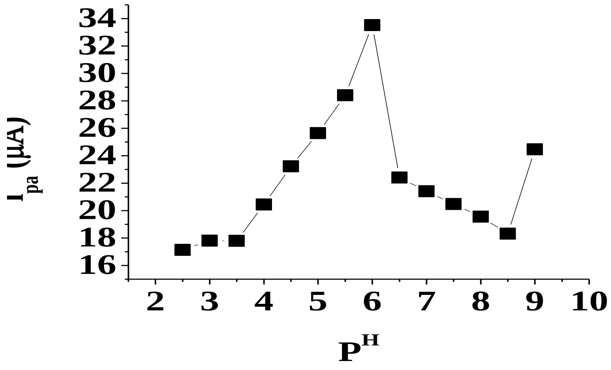
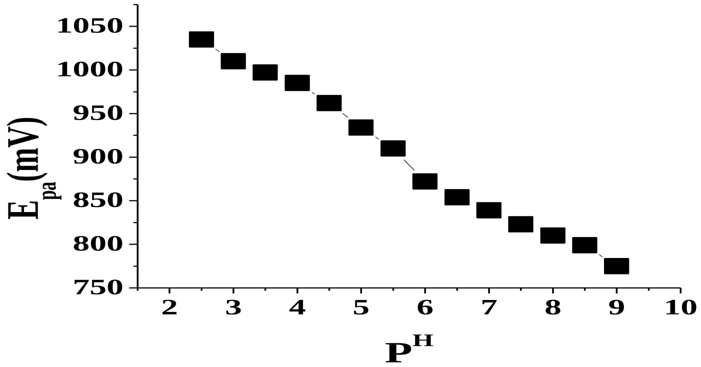


Figure 5b: Plot of anodic peak potential vs. pH (2.5 – 9.0) of 0.1 mM DICY at the poly (TBS) MCPE.

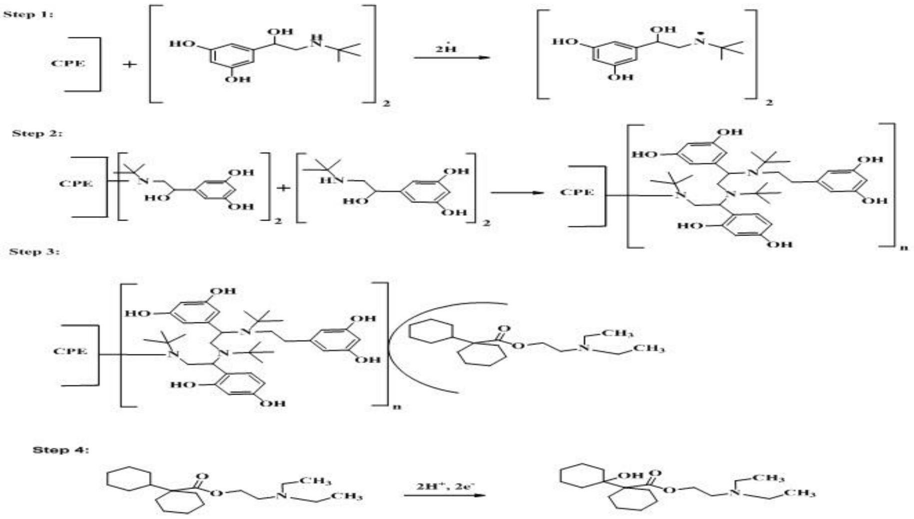


3.7. Effect of scan rate

The effect of scan rates on the electrochemical response of 0.1 mM DICY at poly (Terbutaline Sulphate) modified CPE was studied at different scan rates. Redox peak current increase linearly with the scan rate ($_\gamma$**)** in the range 25, 50, 75, 100, 125,150, 175, 200, 225, and 250,275 and 300 mV/s and the cyclic voltammograms were shown in **Figure 6a** and **Figure 6c** shows linear relationship with a correlation coefficient of R= 0.99737 was obtained between the peak current and square root of scan rate in the range of 25-300 mVs^{-1}, which revealed that a diffusion controlled process occurring at the poly (Terbutaline sulphate) modified CPE. However linearity was also obtained for the plot of scan rate vs. the anodic peak current with a correlation coefficient of 0.992 shown in **Figure 6b**. The relationship between the anodic peak potential and scan rate can be explained by plotting the Anodic peak potentials vs. Natural logarithm of scan rate **(Figure 6d)** by considering the relation: E_{pa}= 0.0918 lnυ +0.62534; R= 0.9817 and the relationship between the anodic peak current and scan rate can be explained by plotting the Logarithm of anodic peak current vs. Logarithm of scan rate **(Figure 6e)** by considering the relation: $\log i_{pa}$= 0.4375logυ +0.2135; R= 0.99672.

According to Laviron's theory [10] the slope is equal to $RT/\alpha n_\alpha F$.

As for a totally irreversible electrode reaction on the basis of the above discussion, the n_α was calculated as 1.6386, which indicated that two electron was involved in the oxidation process of DICY at the poly (Terbutaline Sulphate) modified CPE. Since the equal number of electron and proton took part in the oxidation of DICY, therefore two electrons and two proton transfer were involved in the electrode reaction process. The electrochemical reaction process for DICY at Poly (Terbutaline sulphate) modified CPE can therefore be summarized as in **Scheme III**. From the deduced mechanism of DICY, an intermediate of a free radical was formed. It may be just the free radical polymerizes and comes into being as insoluble products that deposit on the electrode surface, which agrees with the phenomena of voltammograms recorded from multi-cycle [11]



Scheme III: Probable Oxidation Reaction Mechanism of DICY.

Figure 6a: Cyclic Voltammograms of 0.1 mM DICY at the poly (TBS) MCPE with different scan rates were (a) 25, (b) 50, (c) 75, (d) 100, (e) 125, (f) 150, (g) 175, (h) 200, (i) 225, (j) 250, (k) 275, (l) 300 mVs^{-1}.

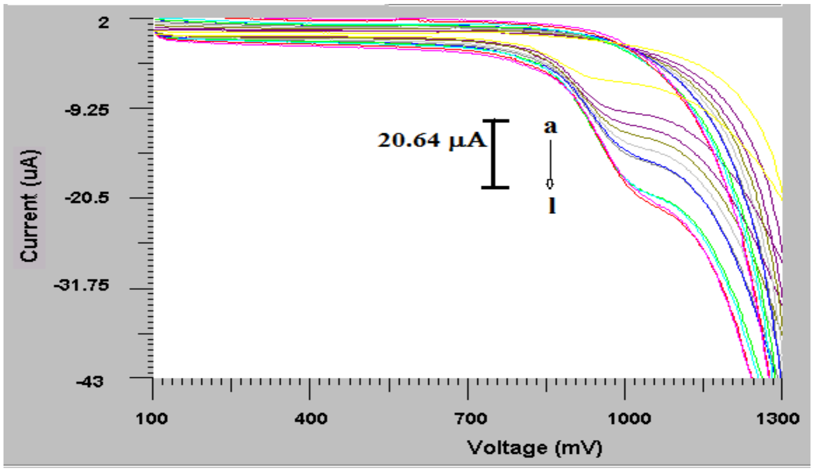


Figure 6b: The plot of Anodic peak current vs. scan rates of DICY at poly (TBS) MCPE.

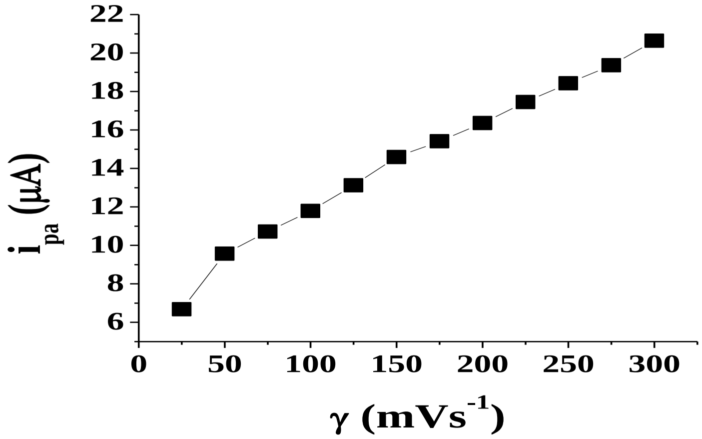


Figure 6c: The Plot of Anodic peak current (i_{pa}) vs. Square root of Scan rates of DICY at poly (TBS) MCPE.

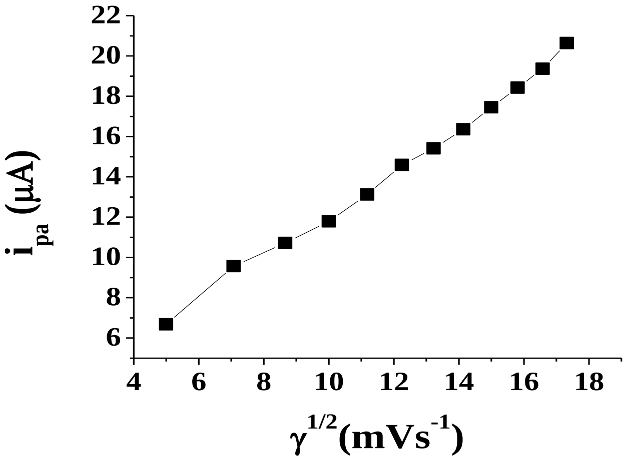


Figure 6d: The Plot of Anodic peak potential vs. Natural logarithm of Scan rates of DICY at poly (TBS) MCPE.

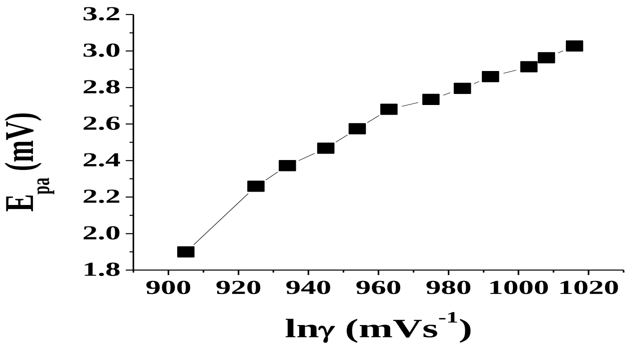
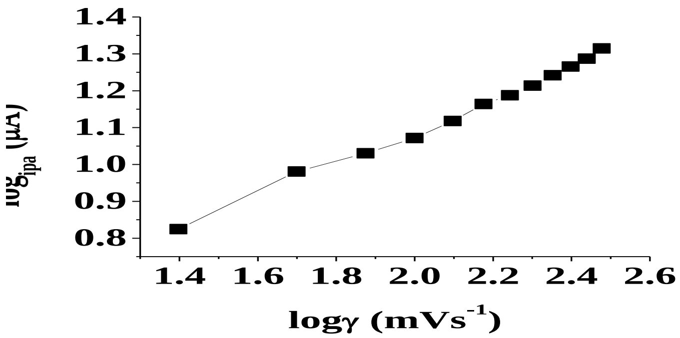


Figure 6e: The Plot of logarithm of Anodic peak current vs. logarithm of scan rates of DICY at poly (TBS) MCPE.



3.8. Effect of Dicyclomine hydrochloride (DICY) concentration and detection limit

Under selected conditions, the effect of DICY concentration on the oxidation peak current was studied by cyclic voltammetry in PBS (pH 6.0) at the scan rate 50 mVs^{-1}.Under the optimum conditions, the oxidation peak current increases with increase in concentration of DICY. **Figure 6a** and **Figure 6b** shows the linear relationship between the oxidation peak current (I_{pa}) with DICY concentration in the range from 1 x10^{-5} M to 1 x10^{-4} M. The linear regression equation: I_{pa} (µA) = 195.726C (10^{-5} M) + 4.4108 (R = 0.99446). The limit of detection (LOD) and limit of quantification (LOQ) of DICY were found to be 0.12 µM and 0.406 µM, respectively.

Related stastical data of calibration curves were obtained from five different calibration curves (n=5). The LOD and LOQ were calculated from the peak current using the following equation:

LOD = 3S/M, ….LOD = 10S/M

Where **S** is standard deviation and M is the slope (Sensitivity) of calibration plot.

Figure 6a: Effect of variation of concentration of DICY (a) 1 X 10^{-5} M, (b) 2 X 10^{-5} M, (c) 4 X 10^{-5} M, (d) 6 X 10^{-5} M, (e) 8 X 10^{-5} M, (f) 1X 10^{-4} M on anodic peak current at poly (TBS) MCPE; υ=50 mVs^{-1}.

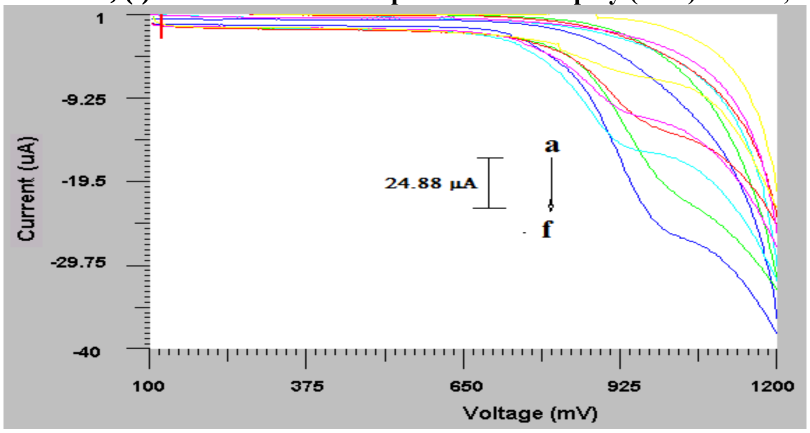
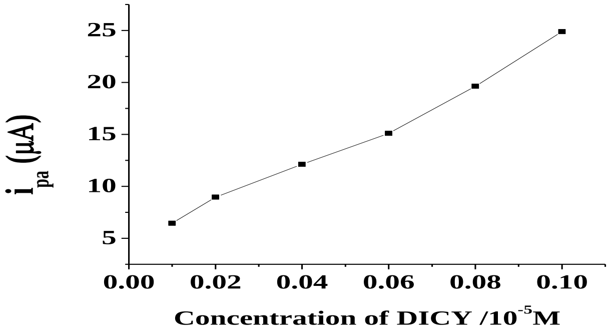


Figure 6b: The plot of Anodic peak current vs. DICY concentration at poly (TBS) MCPE.



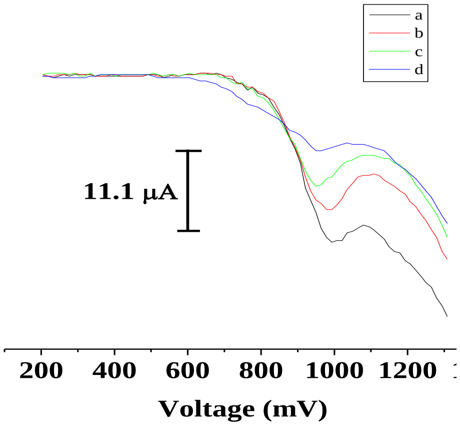
3.9. Dicyclomine Hydrochloride studies by Differential pulse Voltammetry (DPV):

Differential pulse voltammetry (DPV) was used to investigate the possibility of poly (Terbutaline Sulphate) modified carbon paste electrode for determination of DICY. The current responses of this DICY changed by changing the concentrations of DICY. As illustrated in **Figure 7** DPV responses of the modified electrode of DICY increased linearly with increase of their concentrations.

The linear regression equations for DICY in the range of 1×10^{-5} to 4×10^{-5} M is given by,

$$i_{pa}\,(\mu A) = 3.5 + 189C\,(10^{-5}\,M) \qquad (r = 0.9957).$$

Figure 7. DPV of DICY of (a) 1×10^{-5} M, (b) 2×10^{-5} M, (c) 3×10^{-5} M,(d) 4×10^{-5} M.



4. Conclusions

In the present study, a poly (Terbutaline Sulphate) modified carbon paste electrode based on the electropolymerisation has been prepared for the electrochemical determination of Dicyclomine Hydrochloride (DICY). Results showed that the oxidation peak current of Dicyclomine Hydrochloride (DICY) was improved at Poly (Terbutaline Sulphate) modified CPE. The electrochemical response is diffusion controlled and irreversible in nature. A linear concentration range was found to occur from

1 X 10^{-5} to 1 X 10^{-4} M by CV. The probable reaction mechanisms involved in the oxidation of Dicyclomine Hydrochloride (DICY) were also proposed.

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