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Development of an Electroanalytical Method for the Determination Dicyclomine Hydrochloride Using Pencil Graphite Electrode

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Abstract

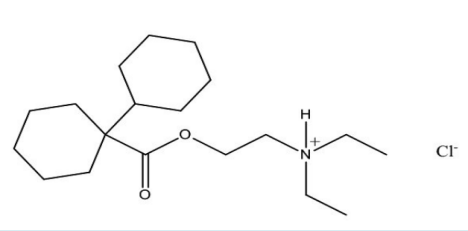
Electroanalytical methods are being used widely for the determination of pharmaceutically active ingredients as they are known for their sensitivity and selectivity. In the present study, the electrochemical behavior of dicyclomine hydrochloride is investigated at pencil graphite electrode for the first time and developed an alternative analytical method for its determination in analyte fortified samples. Dicyclomine hydrochloride exhibited an oxidation peak at 1.023 V in phosphate buffer of pH 7 in the forward scan and no peak in the backward scan suggesting that the electrochemical behavior is irreversible. Influence of pH of phosphate buffer solution and scan rate on electrochemical behavior of dicyclomine hydrochloride is explored. Under optimized conditions, an alternative analytical method is developed for the determination of Dicyclomine hydrochloride in bulk and analyte fortified urine samples. A linear response is observed between anodic peak current and concentration of Dicyclomine hydrochloride in the range of 0.1 to 0.9 µM with the limit of detection of 0.06 µM. Further, practical utility of the developed analytical method was established by determining the Dicyclomine hydrochloride in analyte fortified urine samples. Recovery values is found to be more than 97.14% indicated that the developed method is accurate for Dicyclomine hydrochloride determination.

Keywords: Dicyclomine Hydrochloride; Pencil Graphite Electrode; Analyte Fortified Samples; Alternative Analytical Method; Sensitive Determination

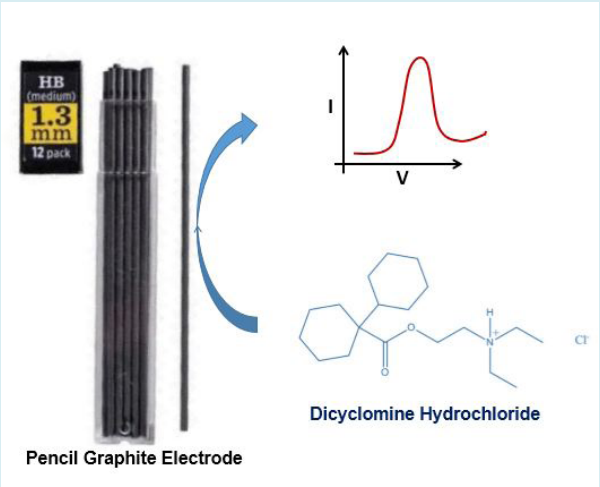
Introduction

Dicyclomine hydrochloride (DH), chemically known as [bicyclohexyl]-1-carboxylic acid, 2-(diethylamino)ethyl ester hydrochloride (Scheme 1), anticholinergic/antispasmodic, being used to treat irritable bowel syndrome.[1-3] Irritable bowel syndrome is a chronic disease that causing abdominal bloating, colics, diarrhea and constipation. DH relaxing the muscles in the stomach and intestines, thus relaxing cramps of the stomach, bladder and intestine [1-3]. DH mechanism of action involves a specific anticholinergic effect at acetylcholine receptor sites and has a direct effect on smooth muscles. Many quantitative analytical methods have been reported for the determination of DH in pharmaceutical dosage forms and biological samples. Off these, spectrophotometric [4-9] chromatographic [10-18] and other methods [19]. However, the reported analytical methods for DH are suffering from either the involvement of tedious and costly procedure or sensitivity and selectivity. The electrochemical methods of analysis are very critical for the determination of many

drugs and other ingredients present in pharmaceutical drug formulations and biological samples as they do not require sample pretreatment.[19] The advancement in electrochemical techniques in the scope of examination and determination of drugs is because of their specificity, high sensitivity and short analysis times compared with other different techniques. The exploitation of carbon-based electrodes, especially the pencil graphite electrode (PGE), for electrochemical measurements has increased tremendously in recent years due to their simplicity, low cost and high sensitivity for the determination of pharmaceutically active ingredients, which is very important in the field of clinical and pharmaceutical analysis. The pharmaceutical activity and metabolic destiny of many drugs can easily be assessed by knowing their redox properties. In view of this, it is planned to explore the electrochemistry of DH at PGE and develop an alternative analytical method for its determination in bulk and analyte fortified biological samples. Scheme 2 demonstrates the use of pencil graphite electrode in investigating the electrochemical behavior of DH and its determination.



Scheme 1: Structure of Dicyclomine Hydrochloride.



Scheme 2: Demonstrates the Use of Pencil Graphite Electrode in Investigating the Electrochemical Behavior of DH and its Determination.

Instrumentation

Potentiostat, CHI 630D electrochemical analyzer (CH Instruments Inc., Austin, TX) was used carry out electrochemical measurements. Three electrode system was used, Ag/AgCl as a reference electrode, a platinum wire as counter electrode and a pencil graphite electrode (PGE) as the working electrode. The pH measurements were made on Elico LI 120 pH meter (Elico Ltd., India).

Reagents and Chemicals

Dicyclomine hydrochloride, purchased from Sigma-Aldrich India, stock solution (1.0mM) was prepared in Millipore water. Phosphate buffer solutions of pH 3 to 11 were prepared by referring Christian and Purdy method Christian GD, et al. [20] other reagents used were of analytical grade. Millipore water was used to prepared all other solutions.

Area of Electrode

The electrochemical active surface area was explored by using cyclic voltammetric technique. In the method 1 mM $K_3[Fe(CN)_6]$ used as a probe. Cyclic voltammograms of 1 mM $K_3Fe(CN)_6$ was recorded for increasing scan rate values. The following Randles - Sevcik equation [21] was useg for reversible process.

$$I_p = (2.69x10^5)n^{3/2}AD_o^{1/2}C\upsilon^{1/2}$$

where I_p is the peak current, n is the number of electrons involved, A is the electroactive surface area, D_0 is diffusion coefficient, υ is the scan rate and C is the concentration of $K_3[Fe(CN)_6]$. For 1.0 mM $K_3[Fe(CN)_6]$, n = 1. D_0 = 7.6 × 10^{-6} cm^2s^{-1}, from the slope of the plot of I_p versus $\upsilon^{1/2}$, the electroactive surface area of pencil graphite electrode was evaluated to be 0.019 cm^2.

Analytical Procedure

The appropriate amount of DH was taken in 2M phosphate buffer solution of pH 7 (10 ml) and then cyclic voltammograms were recorded between 0.0 V and 1.4 V, with a scan rate of 0.1 V s^{-1} to explore the electrochemistry of DH at pencil graphite electrode. Further, square wave voltammetry, initial potential, 0.6 V; final potential, 1.4 V; increase in potential, 0.004 V; amplitude, 0.025 V; frequency, 15 Hz; quiet time, 2s; sensitivity, 1.0×10^{-5} A/V, was utilized for the development of analytical method for the determination of DH in bulk and analyte fortified samples.

Results and Discussion

Electrochemical Behavior of DH

To explore the electrochemistry of DH at PGE, cyclic voltammogram of DH was recorded at PGE in phosphate buffer of pH 7.0. The corresponding voltammograms are shown in Figure 1. DH exhibited an anodic peak at 1.023 V in

the forward cycle and no peak in the reverse scan suggesting that the electrochemical behavior of DH is irreversible. A well-defined anodic peak was noticed might be due to electrocatalytic behavior of PGE.

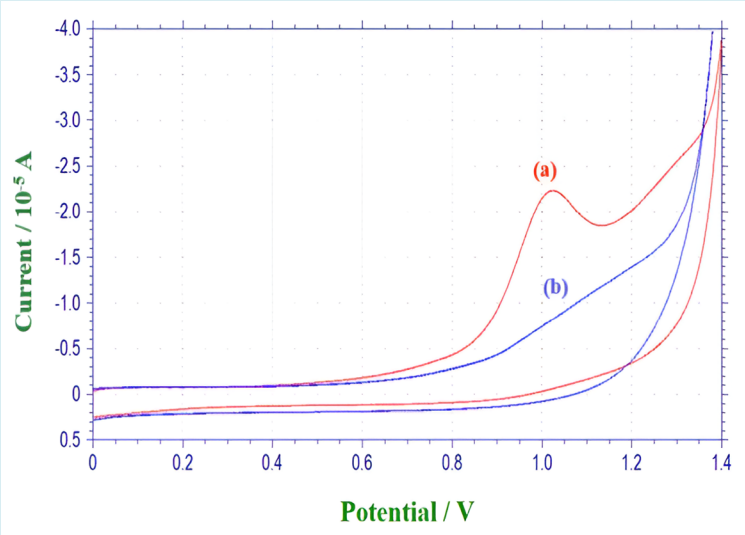


Figure 1: It represents electrochemistry of dicyclomine hydrochloride. (a) Cyclic voltammogram of dicyclomine hydrochloride is recorded at pencil graphite electrode in phosphate buffer of pH 7 at scan rate of 0.1 V/s and (b) control measurement.

Effect of pH on Electrochemical Behavior of DH

Influence of pH on electrochemical behavior of DH was investigated at PGE. Figure 2 displays the cyclic voltammograms of DH at PGE in phosphate buffer of different pH ranging from 3 to 11. As evident from Figure 3 that the oxidation peak of DH shifted towards less positive potentials with increasing pH of phosphate buffer solution indicated that the involvement of protons in the electrode process. The plot E_{pa} vs. pH (Figure 3) yielded a straight line (E_{pa} = 1.2969 - 0.0407 pH; r = 0.9373) with the slope of 40.7 mV/pH which is very close to the theoretical value of 30 mV/pH indicated that the involvement of two electrons and a proton involved in electrode reaction [22-24]. Further, from the plot of I_{pa} vs. pH (Figure 4), it is clear that the DH displayed well-defined oxidation peak with increased peak current in the phosphate buffer of pH 7. Phosphate buffer of pH 7 was used for further studies.

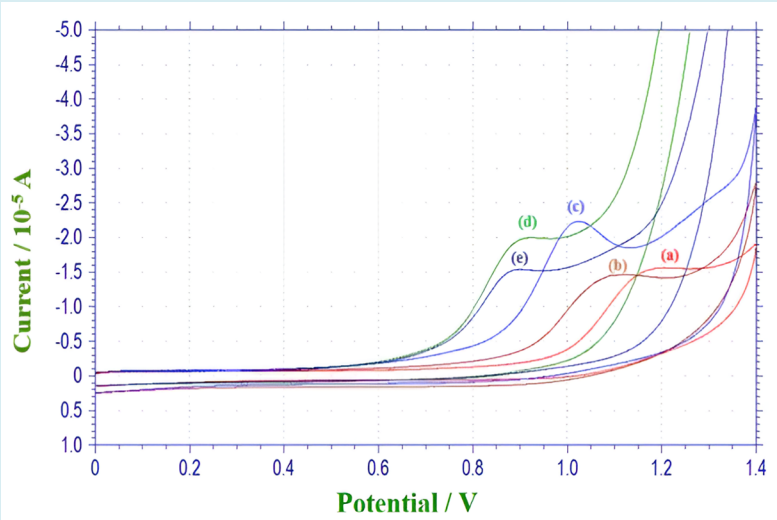


Figure 2: It Represents the Effect of Phosphate Buffer pH on Electrochemical Behavior of Dicyclomine Hydrochloride. Cyclic Voltammograms of 0.5 µM Dicyclomine Hydrochloride is Recorded at Pencil Graphite Electrode in Phosphate Buffer of pH Ranging from 3 to 11 At Scan Rate Of 0.1 V/S (a-pH 3, B-pH 5, C-pH 7, D-pH 9, and E-pH 11).

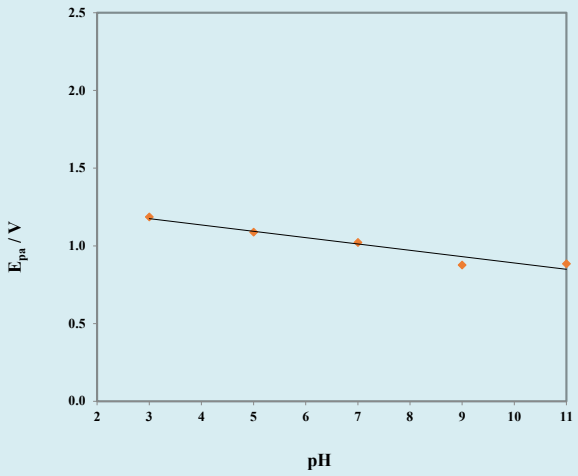


Figure 3: It Represents the Effect of Phosphate Buffer pH on Peak Potential of Dicyclomine Hydrochloride.

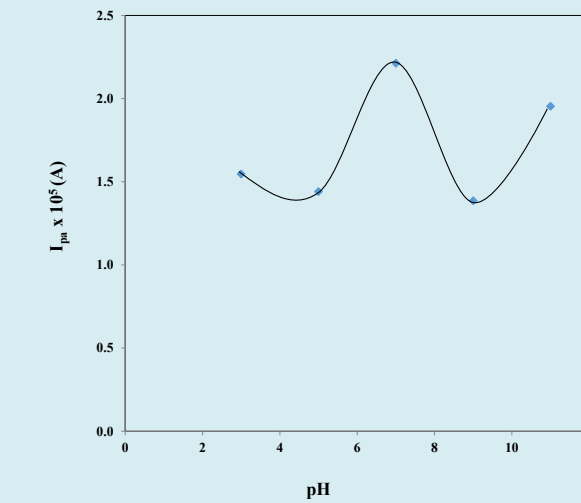


Figure 4: It Represents the Effect of Phosphate Buffer pH on Peak Current of Dicyclomine Hydrochloride.

Influence of Scan Rate on Electrochemical Behavior of DH

The effect of scan rate on electrochemical behavior of DH was investigated in phosphate buffer of pH 7 at different scan rate ranging from 0.1 and 0.3 Vs^{-1}. The corresponding voltammograms are shown in Figure 5. The oxidation peak current of DH linearly increased with increase in the scan rate from 0.1 to 0.3 Vs^{-1} (Figure 6) indicated that the electrode process was found to be adsorption controlled [25]. The corresponding linear regression equation is shown below:

I_{pa} (µA) = 18.416 ν (Vs^{-1}) + 0.2346; (r = 0.9357).

A linear relationship was observed between logI_{pa} and logν (Figure 7) with the slope of 0.83 suggested that the electrode process was adsorption controlled.

I_{pa} (µA) = 0.8287 log ν (Vs^{-1}) + 1.1731; (r = 0.9320)

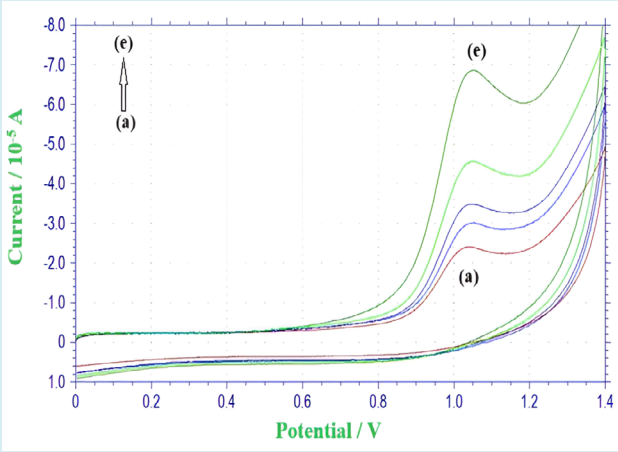


Figure 5: It Represents the Effect of Scan Rate on Electrochemical Behavior of Dicyclomine Hydrochloride. Cyclic Voltammograms Of 0.5 µM Dicyclomine Hydrochloride is Recorded at Pencil Graphite Electrode in Phosphate Buffer of Ph 7 at Different Scan Rate Ranging from 0.1 to 0.3 Vs^{-1}. (a-0.1, b-0.15, c-0.20, d-0.25 and e-0.3 Vs^{-1}).

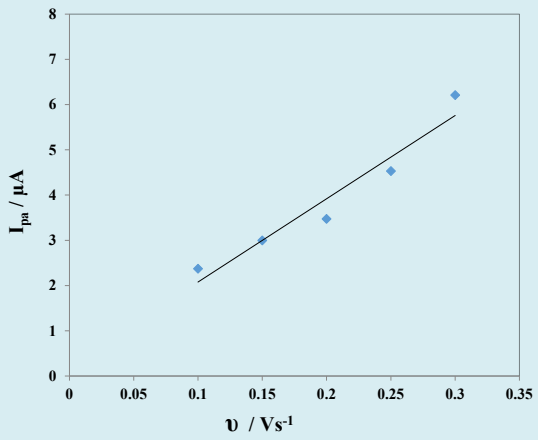


Figure 6: It Represents the Linear Dependence Peak Current of Dicyclomine Hydrochloride on Scan Rate.

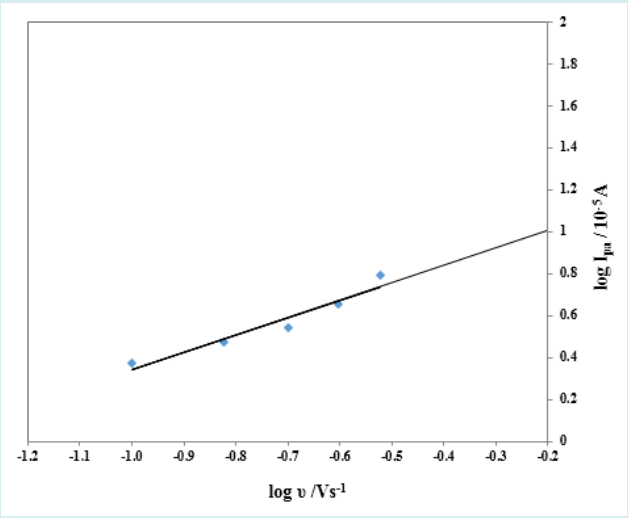


Figure 7: It Represents the Linear logi$_p$ – logν Plot.

Development of Analytical Method

Construction of Calibration Curve

An alternative analytical method was developed for the determination of DH in analyte fortified biological samples. For this, square wave voltammograms was recorded for increasing concentration of DH and corresponding voltammograms are shown in Figure 8.

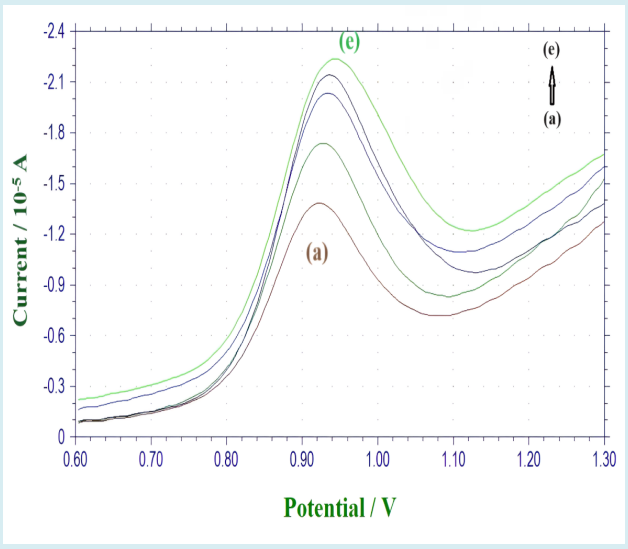


Figure 8: It Represents Square Wave Voltammograms of Dicyclomine Hydrochloride. Square Wave Voltammograms Recorded at Pencil Graphite Electrode in Phosphate Buffer of pH 7 for Increasing Concentration of Dicyclomine Hydrochloride Ranging from 0.1 to 0.9 µm. (a-0.1, b-0.3, c-0.5, d-0.7 and e-0.9 µm).

The linear relationship was obtained between the oxidation peak current and concentration of DH in the range of 0.1 to 0.9 µM (Figure 9). The corresponding regression equation is shown below:

$$I_{pa}\ (\mu A) = 1.4505\mu M + 1.2571;\ (r = 0.9911)$$

The analytical characteristics such as LOD and LOQ was evaluated using the following equations, LOD = 3s/m LOQ = 10s/m, where s is the standard deviation of the peak currents of the blank (five runs) and m is the slope of the calibration curve. LOD and LOQ was found to be 0.06×10^{-6} M and 0.2×10^{-6} M, respectively.

Further, relative standard deviation for intra-day and inter-day was calculated to be less 3.2 % and 2.8 %, respectively suggested that the developed analytical method precise and accurate. Characteristics of calibration plot for DH is tabulated in Table 1.

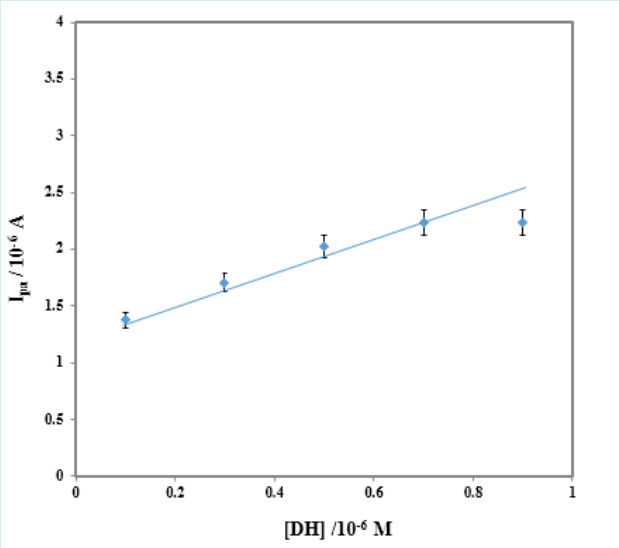


Figure 9: It Represents the Linear Relationship between Peak Current and Concentration of Dicyclomine Hydrochloride.

Analytical method	Square wave voltammetric (SWV) method
Linearity range	0.1 to 0.9 µM
Limit of detection (LOD)	0.06 µM
Limit of quantification (LOQ)	0.2 µM
Inter-day assay RSD* for 0.5 µM	2.80%
Intra-day assay RSD* for 0.5 µM	3.20%

*Average of 5 determinations.

Table 1: Characteristics of Calibration Plot for DH.

Applications of Developed Analytical Method

Determination of DH in Analyte Fortified Biological Samples

The analytical applicability of developed analytical method was established by determining DH in analyte fortified biological urine samples. The recoveries from urine samples were measured by spiking drug free urine with known amounts of DH. The corresponding recovery values were evaluated to be more than 97.14 % indicated that the developed analytical method was accurate and precise for the determination of DH in analyte fortified urine samples. The results of analysis of analyte fortified urine samples is tabulated in Table 2.

DH	DH	DH
added (µM)	found (µM)	recovery (%)
0.5	0.49	98
0.7	0.68	97.14
0.9	0.89	98.88

Table 2: Determination of DH in Analyte Fortified Urine Samples.

Conclusions

Electrochemical behavior of DH was investigated at pencil graphite electrode. DH exhibited an oxidation peak in the forward scan and no peak in the backward scan suggesting that the electrochemical behavior is irreversible. Based on the electrochemical behavior, an alternative analytical method is developed for the determination of DH in bulk and analyte fortified urine samples. Linear response was observed between anodic peak current and concentration of DH in the range of 0.1 to 0.9 µM with the limit of detection of 0.06 µM. Further, practical utility of the developed analytical method was established by determining the DH in analyte fortified urine samples. Recovery values was found to be more than 97.14% indicated that the developed method is accurate for DH determination.

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