

CYCLIC VOLTAMMETRIC STUDY OF LOSARTAN POTASSIUM

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ABSTRACT

Cyclic voltammetric technique has been used for investigation of electrochemical parameters of antihypertensive drug, Losartan Potassium. This drug is usually used for the treatment of blood pressure, type II diabetic disease with proteinuria and stroke prevention. In this study Britton Robinson buffer was used as supporting electrolyte at room temperature 30 ± 1 °C and peak potential (E_p°), Peak current (I_p°), transfer coefficient (α) and diffusion coefficient (D) were estimated at different scan rates, pH and concentration. The electrochemical process was found to be adsorption controlled and irreversible. Furthermore, Losartan Potassium represents transfer of two electrons during reduction reaction.

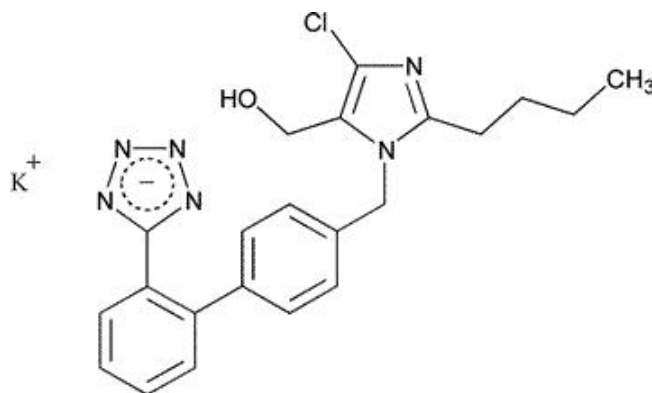
Key word: Cyclic voltammetry, Losartan Potassium, Electrochemical parameters, Gold electrode. Antihypertensive drug

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1. INTRODUCTION:

Losartan Potassium is a member of class I antihypertensive agent [1, 3]. It is effectively used for the treatment of hypertension and heart disease either singly or sometime with the combination of diuretics [1, 2]. It is also recommended for the patient having type II diabetic disease with proteinuria and stroke prevention [5]. This drug is white crystalline, soluble in aqueous medium [4], selective, nonpeptide and angiotensin II receptor antagonist [1].

The IUPAC name of Losartan Potassium is (monopotassium salt) 2-butyl -4-chloro-1-[[2' - (1 H- tetrazol-5-yl) [1, 1'- biphenyl] -4-yl] methyl] - 1H -imidazole -5- methanol [1], with the following structure [3].



Losartan potassium

Literature reveals that the several analytical methods have been used for the qualitative studies of Losartan Potassium such as high performance liquid chromatography (HPLC) [1], high performance thin layer chromatography (HPTLC) [12,8], electrochemical radioimmunoassay [10], reverse phase high pressure liquid chromatography (RP- HPLC) [9,4]. Spectroscopic method was also conducted for determination of Losartan Potassium [6,7] and UV spectroscopic method has been used for the simultaneous estimation of Losartan Potassium and Hydrochlorothiazide (HCT) [10]. Effect of Losartan Potassium on the solubility of Hydrochlorothiazide by solid dispersion technique has been studied [5]. Moreover, electrochemical behavior of Losartan has only been reported by using cathodic stripping voltammetry [12].

Although cyclic voltammetry (CV) is considered as a sensitive and selective method for quantitative and qualitative measurement of various pharmaceutical compounds [12] but according to our knowledge studies related to electrochemical behavior of Losartan Potassium is still limited. Thus, present work has been conducted to investigate the electrochemical properties of Losartan Potassium by estimating peak potential (E_p), peak current (I_p), transfer coefficient (α) and diffusion coefficient (D) of by using CV technique in which gold electrode was used as working electrode.

2. MATERIALS AND METHODS:

2.1 REAGENTS:

A Stock solution of Losartan Potassium (3×10^{-3} mole/dm³) was prepared in 0.04 M Britton Robinson Buffer (B-R). This B-R buffer was prepared in laboratory and used as supporting electrolyte. All other reagents were analytical grade and prepared in double distilled water during the experiment.

2.2 INSTRUMENTATION:

This experiment was performed with CHI- 700 CV and three different electrodes system, a gold electrode as working electrode, a Hg/Hg₂Cl₂ electrode as reference electrode and a platinum wire (Pt) as counter electrode were used. A pH- meter and conductivity meter were also used for monitoring the pH and conductivity respectively throughout the experiment.

2.2 GENERAL PROCEDURE:

The electrochemical cell was filled with 10 ml solution of Losartan Potassium (3mM) and the electrodes (gold electrode, reference electrode and counter electrode) were placed in to the cell to record the voltammograms. The solution was purged with argon gas (99.99%) for 20 min to avoid oxygen interference. The voltammograms of the analyte were recorded at $30 \pm 1^\circ\text{C}$ on computer. During the experiment surface of gold electrode was renewal time to time by polishing with alumina and washing with distilled water. Voltammograms were recorded at the six different scan rate (ν) (20, 100, 200, 300, 400, 500) mV/sec while the range of potential were adjusted from 0 to -1.0 V/sec. Base line of supporting electrolyte was found to be straight at potential (0 to -1.0 V/sec).

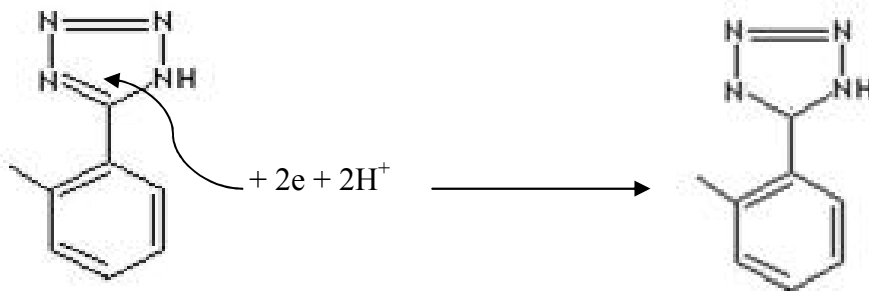
3.0 RESULT AND DISSCUSSION:

This cyclic voltammetric study of Losartan Potassium was carried out in B-R buffer and recorded voltammogram (Fig. 1) represents the first reduction peak at -0.552V with cathodic peak current 1.101×10^{-6} A and the second peak was observed at -0.828V with cathodic peak current 1.739×10^{-6} A. The third peak (reverse peak) was observed only at pH 11 and within the range of 300-500 mV/S scan rate.

3.1 REACTION MECHANISM:

The structure of Losartan Potassium molecule contains imidazole and tetrazolyl group. The imidazole group can be reduced in organic media at ca. -1.77 V while tetrazolyl group can be reduced in alkaline media. [12]. In present study CV profile of Losartan Potassium were also recorded in alkaline medium (pH 8 to 11) which represents the two waves in voltammogram indicating the occurrence of reduction process due to addition of two electrons and two protons at azomethane group $\text{C}=\text{N}$ in tetrazolyl group (Scheme-1) as described in previous report.[12].

Scheme-1



3.2 EFFECT OF SCAN RATE:

A linear trend was observed between the peak currents (I_{pc}^1 & I_{pc}^2) and the square root of the scan rates with strong correlation coefficient (0.993) for the first peak current and (0.994) for second peak current. The plot between the $\log I_{pc}^1$ and I_{pc}^2 and square root of the scan rates ($v^{1/2}$) showed the slope value 0.512 and 0.621 for I_{pc}^1 and I_{pc}^2 respectively, which is close to theoretical value 1.0 which represents the an ideal adsorption controlled electrode process [11,14]. The linear relationship was observed between peak potentials (E_{pc}^1 & E_{pc}^2) and square root of scan rates. (Fig-3) which also indicates the occurrence of irreversible chemical process on electrode [11]. Furthermore, the shape factor $|E_{pc} - E_{p/2}|$ for irreversible reaction system is given by [16]

$$|E_{pc} - E_{p/2}| = 48/\alpha_c n_a \text{ mV} \text{ ----- (1)}$$

In this equation α_c is transfer coefficient and n_a is number of electrons. This equation (1) can also be written as

$$n_a = 48/|E_{pc} - E_{p/2}| \alpha_{cs} \text{ mV} \text{ ----- (2)}$$

Thus, the numbers of electrons were calculated using the values $|E_{pc} - E_{p/2}|$ given in (table-2) and by estimation of α as describe by Bard and Faulkner [13]

$$\alpha = 47.7/|E_{pc} - E_{p/2}| \text{ ----- (3)}$$

Diffusion coefficient (D) (Table-3) was calculated by *Randles Sevcik* equation [11] which is given below

$$I_p = - (2.6 \times 10^5) n^{3/2} C A D^{1/2} v^{1/2} \text{ ----- (4)}$$

3.3 EFFECT OF CONCENTRATION:

The I_p^c represents the linear relationship with different concentration of Losartan Potassium (Fig.4). This linear relationship between I_p^c and concentration with intercept zero indicating that the electron transfer process was adsorption controlled process [2].

3.4 EFFECT OF PH:

The linear decreasing trend in I_p^c has been observed as the pH of B-R buffer increases from 8 to 11 at 100mV/S scan rate (Fig-5). Such trend representing the increase in pH of B-R buffer may affect the solubility of Losartan Potassium and contribution of proton may involved in reduction process which results decrease in the peak current.

3.5 DIAGNOSTIC TEST FOR REVERSIBILITY:

In present work diagnostic test for quasi reversible system (Table-1) [11] are not fully satisfied by Losartan Potassium and only the last criteria for of diagnostic test that is E_p^c shifts negatively with increasing scan rate (Fig-1) followed by Losartan Potassium.

3.6 DIAGNOSTIC TEST FOR IRREVERSIBILITY:

CV profile of losartan potassium at pH 8, 9 and 10 showed the absence of reverse peak which is considered as marked feature of irreversible system. Moreover, second and third criteria for diagnostic tests [11] for irreversible reaction were also fulfilled by the Losartan Potassium (Fig-1&2).

4.0 CONCLUSION:

This cyclic voltammetric study was conducted by adjusting the different physiochemical parameters such as pH, scan rate, concentration to define the electrochemical properties of Losartan potassium. Results suggest that the Losartan Potassium gives the irreversible reaction by following the maximum criteria of irreversible reaction system with two electrons transfer mechanism. Moreover, this reaction process indicates adsorption controlled and reduction process.

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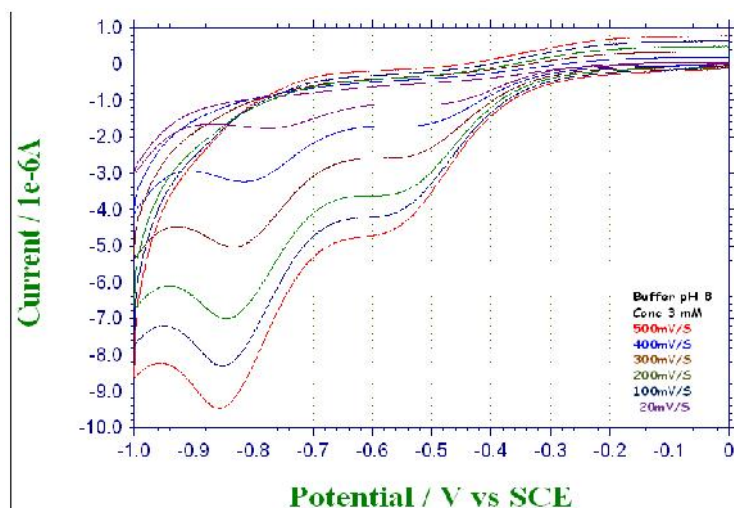


Figure 1: Cyclic voltammograms of 3mM Losartan Potassium at gold electrode Vs SCE reference electrode with different scan rates in presence of Britton Robinson buffer at pH 8 at $30\pm 1^\circ\text{C}$.

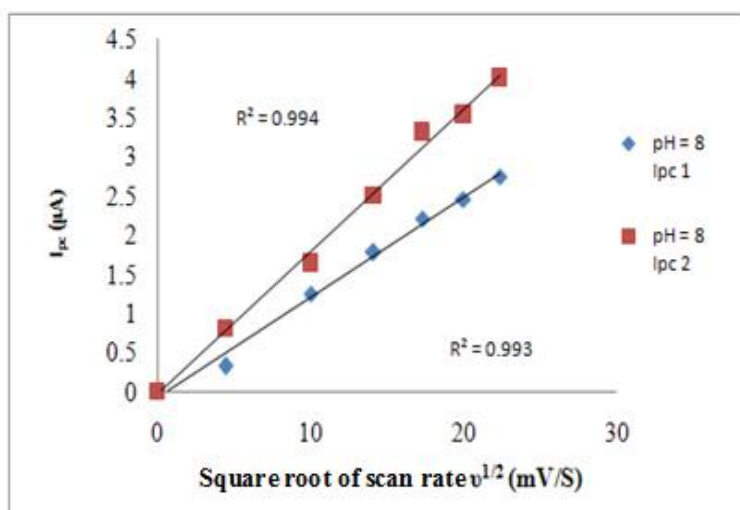


Figure: 2 Relationship of I_{pc}^1 and I_{pc}^2 vs square root of scan rate ($v^{1/2}$) at $30\pm 1^\circ\text{C}$.

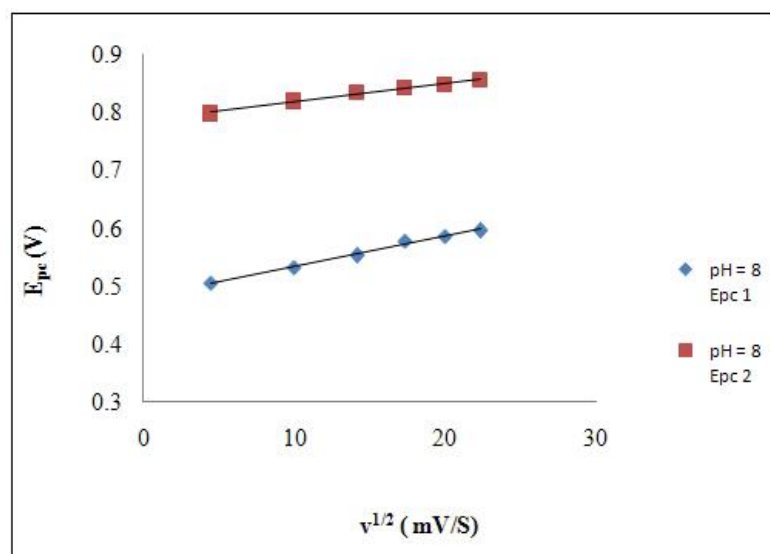


Figure: 3 Relationship of E_{pc}^1 and E_{pc}^2 Vs square root of scan rates ($v^{1/2}$) .

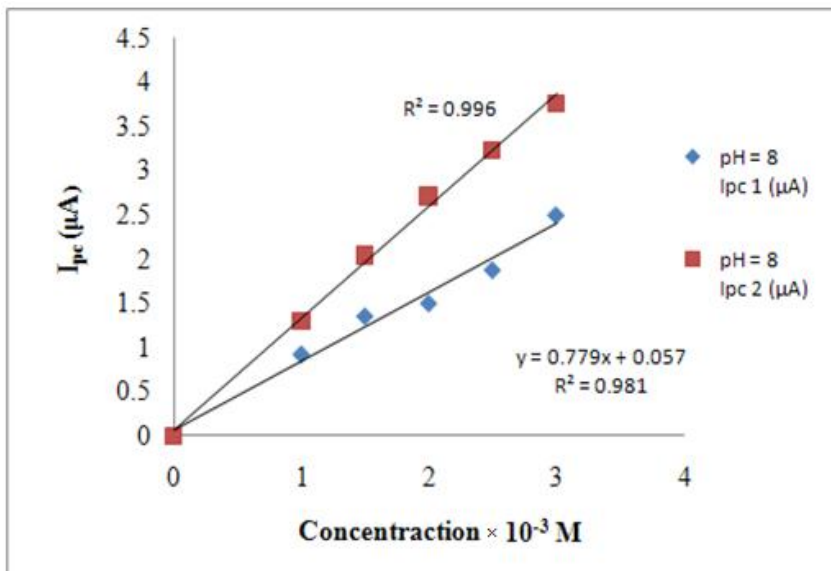


Figure 4 Relationship of I_{pc}^1 and I_{pc}^2 vs concentration of Losartan Potassium at 100 mV/S.

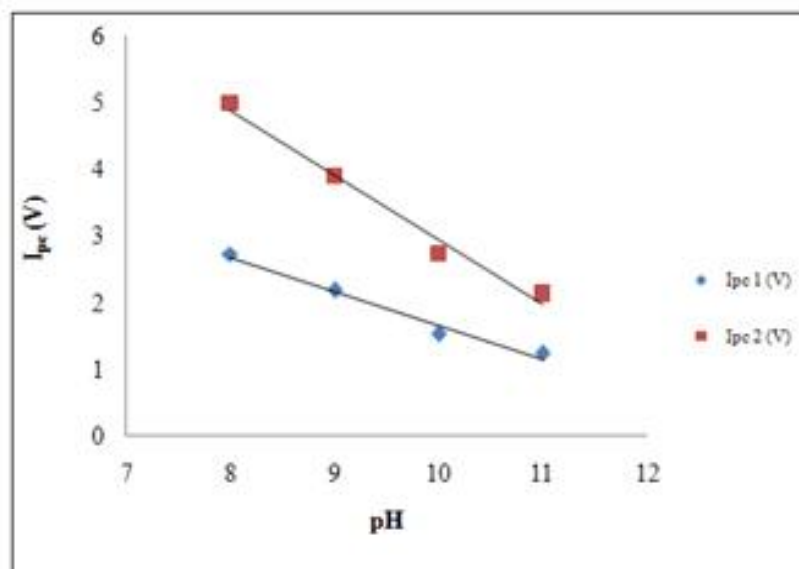


Figure 5 Relationship of I_{pc}^1 and I_{pc}^2 Vs of pH of Britton Robinson Buffer at 100mV/S scan rate.

Table: 1 Diagnostic test for quasi reversible system

- | | |
|---|---|
| 1 | $ I_p $ increases with $u^{1/2}$ but not proportional to it |
| 2 | $ I_p^a/I_p^c = \text{provided } \alpha_c = \alpha_a = 0.5$ |
| 3 | ΔE_p is greater than 59/nmV and increases with increasing u |
| 4 | E_p^c shift negatively with increasing u |
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Table 2: The value of E_{pc}^1 & E_{pc}^2 and I_{pc}^1 & I_{pc}^2 from the cyclic voltammogram of Losartan Potassium 3×10^{-3} mole /dm³ in B-R buffer (pH =8) used as supporting electrolytes with different scan rates at 30°C.

Peak ¹					
Scan rates (mV/S)	E_{pc}^1 (mV/S)	$E_{p/2}$ mV/S)	$E_p-E_{p/2}$ (mV/S)	$\alpha = 48/E_p-E_{p/2}$	$I_{pc}^1 \times 10^6$ (μA)
20	503.5±2.94	430.7±1.15	72.73±2.57	0.66±0.02	0.93±0.01
100	532.2±0.53	456.23±0.06	75.97±0.59	0.63±0.00	1.77±0.01
200	552.73±0.06	452±0.61	100.73±0.59	0.47±0.00	2.562±0.02
300	577.2±0.10	462.8±0.10	114.4±0.17	0.42±0.00	3.61±0.01
400	586.93±0.06	470.63±0.51	116.3±0.46	0.41±0.00	4.23±0.04
500	595.2±0.10	472.4±0.10	122.8±0.20	0.40±0.00	4.67±0.01
Peak ²					
Scan rates (mV/S)	E_{pc}^2	$E_{p/2}$	$E_{pc}-E_{p/2}$	$\alpha = 48/E_{pc}-E_{p/2}$	$I_{pc}^2 \times 10^6$ (μA)
20	798.1±0.09	704.4±0.11	93.6±0.05	0.512±0.00	0.621±0.00
100	818.8±0.53	737.2±0.12	81.5±0.64	0.58±0.00	1.542±0.00
200	834.1±0.10	743.63±0.06	90.46±0.15	0.53±0.00	2.104±0.01
300	843.1±0.10	753.6±0.10	89.5±0.10	0.54±0.00	3.318±0.00
400	847.1±0.06	761.5±0.26	85.67±0.31	0.56±0.00	3.87±0.01
500	856.1±0.06	768.2±0.10	87.967±0.15	0.55±0.00	4.242±0.00

Table 3: Values of α , Diffusion coefficient, R^2 and Slope of I_{pc}^1 of 3mM of Losartan Potassium at different pH of B-R buffer at 100mV/S.

Peak ¹					
S.No	pH	α	"D" (cm ² /s) 10 ⁵	Slope "m" 10 ⁻⁶	R^2
1	8	0.637±0.001	0.8705±0.01	0.174±0.01	0.999±0.01
2	9	0.630±0.02	0.1295±0.01	0.246±0.01	0.962±0.01
3	10	0.515±0.02	0.1887±0.01	0.224±0.01	0.987±0.02
4	11	0.654±0.01	0.1882±0.01	0.148±0.01	0.980±0.02
Peak ²					
S.No	pH	α	"D" ^{1/2} (cm ² /s) 10 ⁵	Slope "m" 10 ⁻⁶	R^2
1	8	0.585±0.01	1.133±0.01	0.208±0.01	0.997±0.01
2	9	0.625±0.02	2.051±0.015	0.561±0.01	0.993±0.01
3	10	0.782±0.015	3.438±0.021	0.542±0.01	0.994±0.12
4	11	0.8421±0.01	0.955±0.01	0.339±0.12	0.987±0.01

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