

**Research Paper**

**CYCLIC VOLTAMMETRIC STUDY OF LOSARTAN POTASSIUM**

**ABSTRACT**

Losartan Potassium has a significant role in lowering blood pressure. In the present study various electrochemical parameters such as  $E_p$ ,  $E_{p/2}$ , ( $\alpha$  transfer coefficient) were determined at different scan rates in BR buffer. Similarly the effect of pH/ concentration of analyte and influence of repeated scans were also studied at a gold disk test electrode Vs saturated calomel (SCE) reference electrode at  $30 \pm 1^\circ \text{C}$ . It was found that the CV profiles of losartan potassium showed a two electron transfer reduction process which was significantly altered by changing pH. The method was validated both for qualitative and quantitative determination of losartan Potassium.

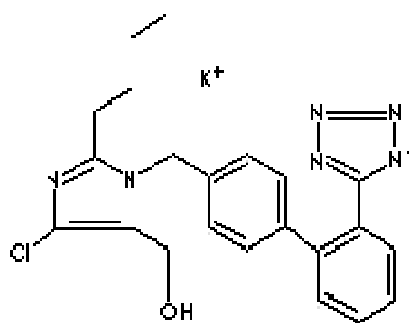
Key word:

Losartan Potassium, electrochemical parameters, Transfer coefficient, BR buffer, C.V. Study at gold electrode test electrode.

INTRODUCTION:

Losartan potassium belongs to class I antihypertensive agent [3]. It is effectively used for the treatment of moderate or severe hypertension and heart disease either singly or some time with diuretics [1,2]. Losartan potassium is very selective, nonpeptide angiotensin II receptor antagonistic [1]. The dosage of losartan potassium increases the plasma rennin activity which causes elimination of angiotension II feedback [1]. It is also used for the protection of type II diabetic disease for patients with proteninuria and stroke prevention.

Losartan potassium is white crystalline fine powder soluble in aqueous medium which is metabolized in liver. Molecular formula of losartan potassium is  $C_{22}H_{22}Cl KN_6OH$ . The molecular mass of losartan potassium is 461.01gm/ mol. It is monopotassium salt commonly known as Losartan potassium. The I.U.P.A.C name of monopotassium salt is 4-butyl -4-chloro-1- {[2' - (1 H- tetrazol-5-yl)[1, 1' - biphenyl} -4-yl]methyl} - 1H -imidazole - 5- methanol [ 5-9].



Losartan potassium

Literature reveals that several analytical methods have been used for the qualitative studies for losartan potassium like HPLC, HPTLC, electrochemical radioammonoassay, The

simultaneous estimation by first order derivative spectroscopy [5] and HCT [13-15] were used to study singly and in combination with hypertensive diuretics drugs. The reverse phase high pressure liquid chromatography (RP- HPLC), and thin layer chromatography method [5] including spectrophotometric determination and cathodic stripping voltammetry by using mercury dropping electrode have also been carried out in acidic medium. However no cyclic voltammetry has yet been reported so far in the literature on losartan potassium.

Cyclic voltammetry is selective, sensitive, and versatile technique used for method validation, as well as for quantitative and qualitative measurement of some of the pharmaceutical significant compounds.

In the present work cyclic voltammetry was performed at Gold test electrode for the determination of electrochemical parameters of losartan potassium.

#### **Experimental:**

CHI- 700 Cyclic Voltammeter was used for recording voltammograms of the analyte using Gold electrode (Au) as a test electrode, V/S Hg/Hg<sub>2</sub>Cl<sub>2</sub> electrode as reference and Platinum (Pt) as counter electrode. A pH- meter (Jenvay) was also used for monitoring the pH of solution. Conductivity meter HANNA (HI- 8633) (Romania) was used for conductivity measurements.

#### **Reagents:**

Robinson buffer (Laboratory prepared) was used as supporting electrolyte comprising Boric acid, Acetic Acid, and phosphoric acid. A Stock solution of Losartan potassium of  $3 \times 10^{-3}$  mole/dm<sup>3</sup> (E.Merk) was prepared in 0.04 M BR- Buffer. All reagents used were of analytical grade and were prepared in double distilled water.

#### **General procedure:**

In electrochemical cell took 10 ml of the solution. Connected the three electrodes gold as test electrode, platinum as counter and Hg/Hg<sub>2</sub>Cl<sub>2</sub> as reference electrode with potentiostat. Argon gas (99.99%) pure was purged for 20 min for inert atmosphere. The voltammogram of the analyte were recorded at 30±1°C. To avoid the contamination of the surface of gold test electrode it was renewed with polishing material and washed with distilled water several times and drying with watman filter paper.

**Base line:** The parameters like initial potential, signal potential, and the scan rate etc. were adjusted before taking C.V. in the pure supporting electrolytes for taking the base line. The Base lines in the supporting electrolyte were horizontally straight. After taking base line at a given scan rate the analyte in that supporting electrolyte was analyzed by taking cyclic voltammetry. Each reading was taken three times for their average data analysis purpose.

## **Result and discussion:**

Qualitative study of losartan potassium was carried out in basic medium of R-B buffer in different pH- range (8-11). Voltammograms of losartan potassium were taken at different potential scan rates ranging from 20-500mV/s at gold test electrode in the applied potential range 0 - -0.1 Volt as shown in figure 1. The first peak of analyte appeared at -0.552 V (with cathodic peak current  $1.101 \times 10^{-6}$   $\mu$ A). The second peak at -0.828 V (with cathodic peak current  $1.739 \times 10^{-6}$   $\mu$ A). One reverse peak appeared at pH 11 and scan rates. This is shown in Fig 2.

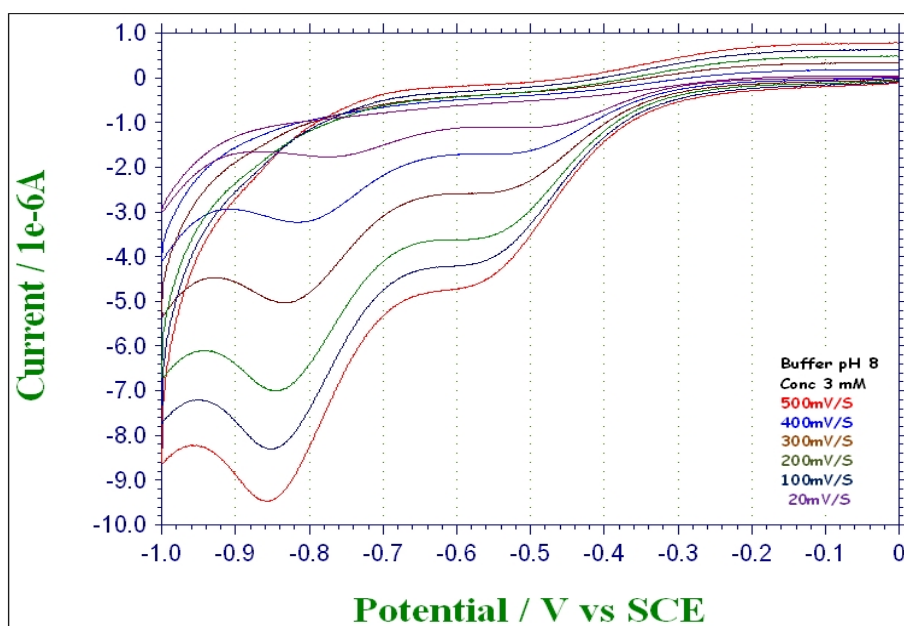


**Figure 1:** First scan cyclic voltammograms of 3 mM losartan potassium at gold test electrode Vs SCE reference electrode with different scan rates in presence of Robinson buffer at pH 8 used as supporting electrolytes at  $30\pm 1^\circ\text{C}$ .

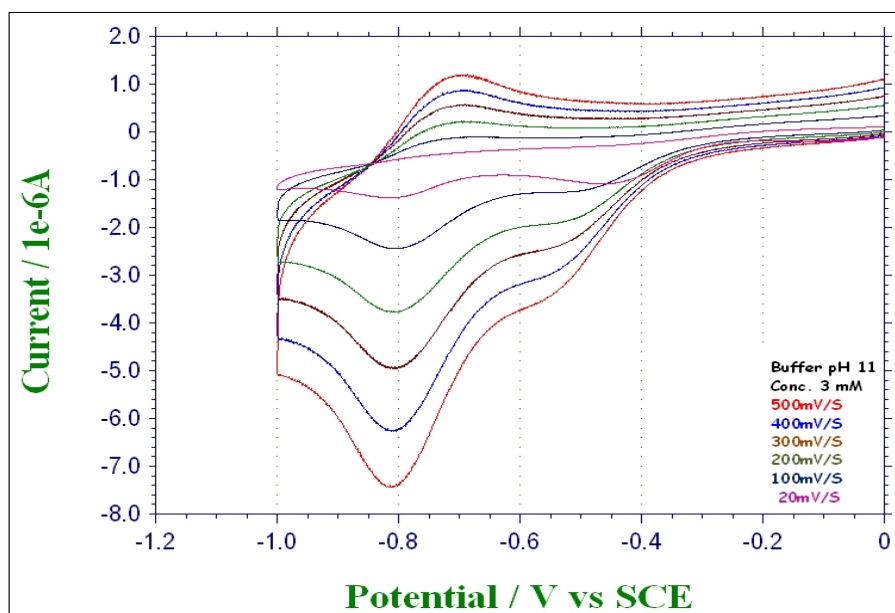
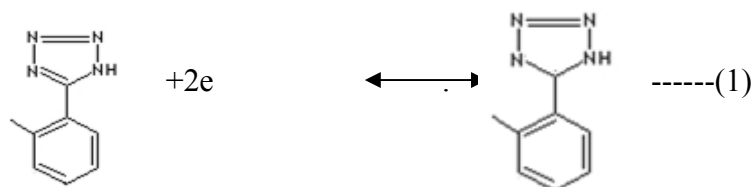


**Figure 2:** first scan cyclic voltammograms of 3 mM losartan potassium at gold test electrode Vs SCE reference electrode with different scan rate in presence of Robinson buffer pH 11 used as supporting electrolytes at  $30\pm 1^\circ\text{C}$

## 112 **Reaction Mechanism:**

113           Structure of losartan potassium molecule contains imidazole group and tetrazolyl  
 114 group. These functional groups do not easily reduce electrochemically while providing  
 115 potential to the gold test electrode in aqueous medium [17]. However at high pH >7 such  
 116 annalyte can be reduced at the surface of test electrode due to the presence of halide group  
 117 [18]. The possible mechanism of electrode reaction carried out on the surface of the test  
 118 electrode can be assigned to proton transfer reaction which is actually coupled to electron  
 119 transfer hence reduces azomethine group C=N in tetrazolyl group into saturated bond  
 120 involving 2 electrons and 2 protons. This is also confirmed by the present CV profiles where  
 121 two waves appeared due to the two electrons transfer process. The same was reported in  
 122 literature [17]. This is represented in equation 2.

123



## 127 **Effect of scan rate:**

128           The effect of scan rate on  $I_p$ ,  $E_p$ ,  $E_{p/2}$  of losartan potassium was studied. Here a linear  
 129 trend was observed between the reduction peak currents ( $I_{pc}^1$  &  $I_{pc}^2$ ) and the square root of  
 130 the scan rates which is shown in Fig 3. The plot of  $I_{pc}$  V/s  $v^{1/2}$  passed through origion which  
 131 confirms that this is adsorption controlled process [17] . The Value of  $r^2$  (0.994) statistically  
 132 representing the strong relationship between  $I_{pc}$  V/s  $v^{1/2}$ . The Second reduction peak current  
 133 also showed a linear pattern  $I_{pc}^2$  V/s square root of scan rates, However it remain in peak

shape at high scan rates with significant correlation coefficient of 0.993 and slope value obtained  $0.208 \times 10^{-6}$ .

In case of irreversible process the value  $E_{pc}$  generally shifts towards negative potential range [16]. In this case the same trend was obtained in the voltammogram of losartan potassium at different scan rates (20, 100, 200, 300, 400, 500 mV/S), which is shown in figure 4. The values of transfer coefficient  $\alpha$  were calculated by using equation 2. According to Bard and Faulkner [ ]  $\alpha$  can be calculated by the equation.

$$\alpha = 47.7 / (E_{pc} - E_{p/2}) \quad (2)$$

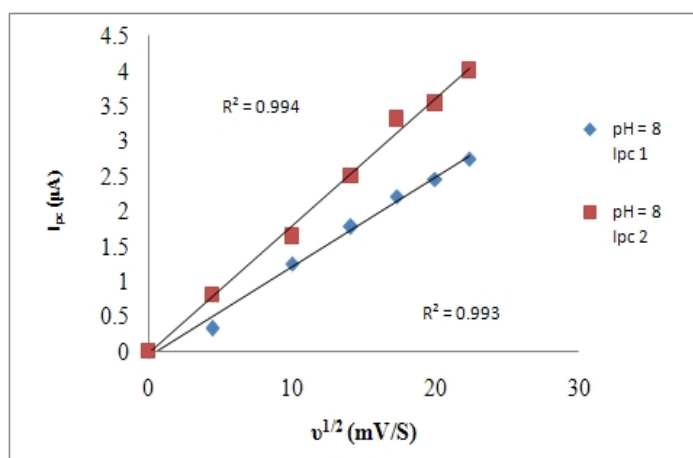


**Figure: 3** The plot of  $I_{pc}^1$  and  $I_{pc}^2$  Vs square root ( $v^{1/2}$ ) of potential scan rates in (pH=8) buffer at  $30 \pm 1^\circ C$ .

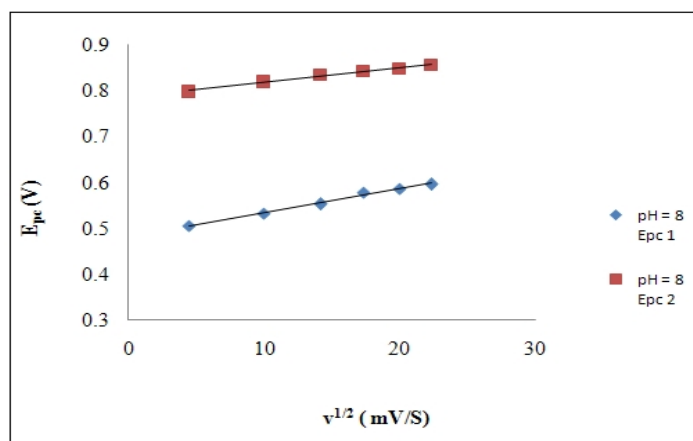


**Figure: 4** The plot of  $E_{pc}^1$  and  $E_{pc}^2$  Vs square root ( $v^{1/2}$ ) of potential scan rates at in (pH=8) buffer  $30 \pm 1^\circ C$ .

## Effect of concentration

The effect of concentration on peak current of analyte was also studied in 0.04M BR- buffer in different pH range from (8-11), used as a supporting electrolyte. The values of  $E_{pc}^1$  and  $E_{pc}^2$  are found to be independent of change in concentrations range ( $1 \times 10^{-3}$  to  $3.5 \times 10^{-3}$  M) of analyte at 100mV/S scan rate. It represented in Fig 5. The Value of  $I_{pc}$  Vs concentration range ( $1 \times 10^{-3}$  - $3.5 \times 10^{-3}$  M) of analyte passed through origin which was confirmed that this is diffusion controlled process. This is shown in figure 6.

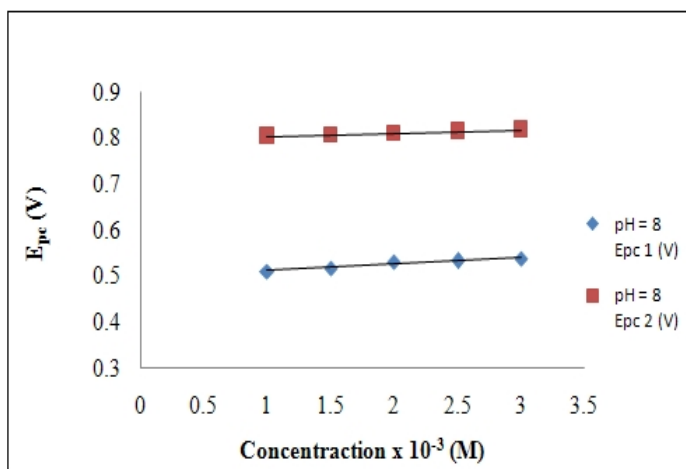


**Figure: 5**

The plot of  $E_{pc}^1$  and  $E_{pc}^2$  Vs concentration of analytes at 100mV/S at  $30 \pm 1^\circ\text{C}$ .

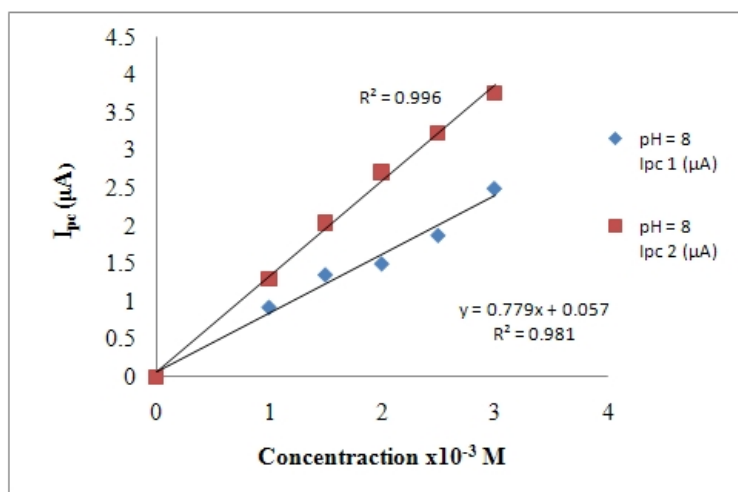


**Figure: 6**

The plot of  $I_{pc}^1$  and  $I_{pc}^2$  Vs concentration of analyte at 100mV/S at  $30 \pm 1^\circ\text{C}$ .

The repeated scan rates of 3mM concentration of losartan potassium at 100 mV/S showed that greater product adsorption occurred in terms of reduction of proton at a gold electrode surface as compared to adsorption and desorption of “H” explained by Greef et al (1985). [16]. This is given in Fig 7

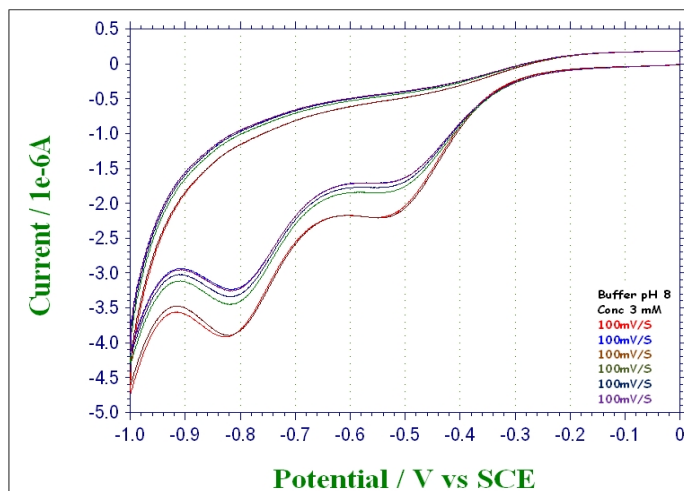


**Figure 7:** Repeated scan cyclic voltammograms of 3 mM losartan potassium at gold test electrode Vs SCE reference electrode taken at 100mV/S scan rate in presence of Robinson buffer (pH = 8) at  $30 \pm 1^\circ\text{C}$ .

### Effect of pH:

The Effect of pH on electrochemical parameters of losartan potassium was also studied here. C.V. profiles of 3mM concentration of losartan potassium were taken in different pH of Robinson buffer at 100mV/S scan rate. An insignificant change in  $E_{pc}^1$  and  $E_{pc}^2$  was found with the increase in pH of Robinson buffer which is shown in fig 8 and 9. The Same pattern was observed in peak current ( $I_{pc}^1$  and  $I_{pc}^2$ ) which significantly decreased with increasing the pH of buffer solution shown in Fig 10. The change in  $E_{pc}$  with pH represents that low conc. of analyte is available for reduction on the surface of gold disk electrode. This

may be due to the slow diffusion process of analytes from the bulk of the solution to the test electrode surface which was also reported earlier [16].

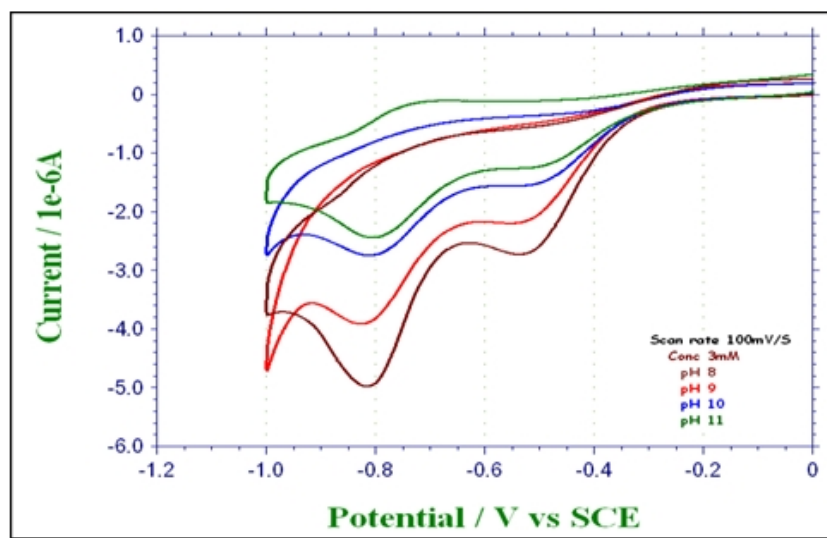


**Figure 8:** cyclic voltammograms of 3mM losartan potassium at gold electrode Vs SCE reference electrode 100mV/S scan rate in presence of Robinson buffer pH (8-11) used as supporting electrolytes at 30±1°C.

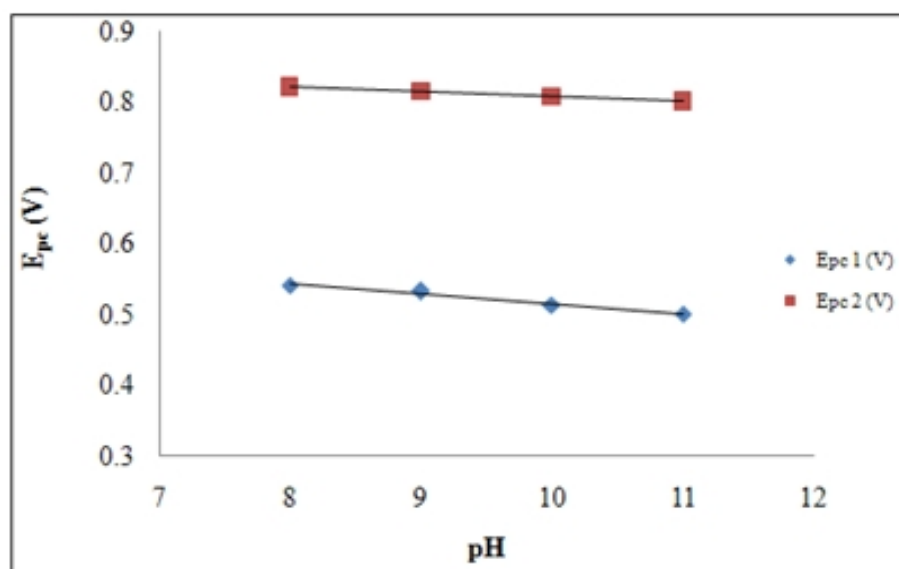


**Figure: 9** The plot of  $I_{pc}^1$  and  $I_{pc}^2$  Vs pH BR-Buffer at 100mV/S scan rate at 30±1°C.

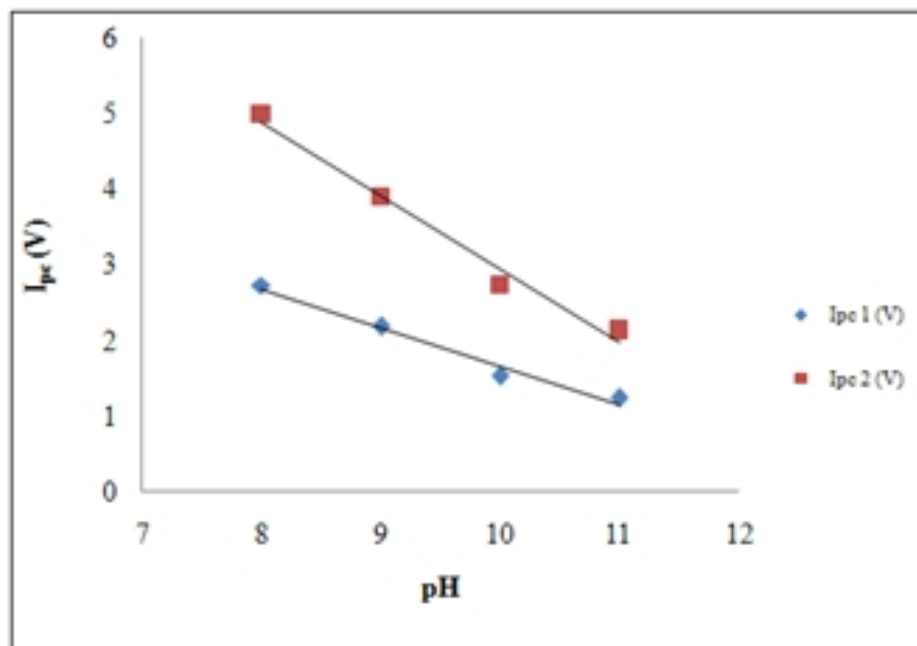


**Figure: 10** The plot of  $E_{pc}^1$  and  $E_{pc}^2$  Vs of pH of BR-Buffer at 100mV/S scan rate at  $30 \pm 1^\circ\text{C}$ .

#### Diagnostic test for reversibility:

The reported diagnostic tests were applied to confirm the characterization of losartan potassium in Robinson buffer system in different pH range (8-11). It partially fulfilled the diagnostic test of quasi reversible systems [16]. The criteria for a quasi reversible process is that the  $I_p$  values increases with  $v^{1/2}$  but not proportional but incase of losartan potassium  $I_{pc}$  values are directly proportion to the square root of the scan rates. Secondly the ratio of  $I_{pa}/I_{pc}$  should be "1" provided  $\alpha_a = \alpha_c = 0.5$  Incase of losartan potassium the ratio of  $I_{pa}/I_{pc}$  is  $< 1$  within the limits of experimental error as briefly explained by Greef et al (1985). Thirdly  $\Delta E_p$  is greater than  $59/n$  mV and increases with increasing scan rates. But in case of losartan potassium at low scan rate  $\Delta E_p$  was found to be lesser than  $59/n$  mV and at high scan rates  $\Delta E_p$  values  $> 59/n$  mV and increases with rate of potential scan by Renmuth (1962)

and Bard &Flukner (1980). Finally the peak potential was shifted cathodically by increasing the scan rates according to the criteria of quasi reversible process.

### **Diagnostic test for irreversibility:**

CV profile of losartan potassium at pH 8 and 9, at low scan rate follow the criteria of irreversibility where no reverse peak appeared at low scan rates. A linear trend was also found in Cathodic current with increasing the square root of scan rates.  $E_{pc}$  shifts  $-30/\infty_c n_a$  for each decades. The difference of  $|E_{pc} - E_{p/2}|$  was found to be greater than  $48/\infty_c n_a$ . In casr of losartan potassium almost full fill the ceritria of irreversibility [16].

### **Conclusion:**

It was finally conclude that the CV profiles of losatran potassium was performed at gold as test electrode Vs saturated calomel electrode  $Hg | Hg_2Cl_2$  reference electrode at  $30 \pm 1^\circ C$ . Which Showed two electron transfer process. It fulfils the diagonestic test of irreversible process with gold test electrode. Base line obtained at this electrode was found to be horizontally straight. The qualitative and quantitative characteristics of losartan potassium were studied in 0.04 M Robinson buffer which was used as supporting electrolytes where  $E_p$ ,  $E_{p/2}$ , , diffusion coefficient (D), ( $\infty$  transfer coefficients) were determined at different scan rate at pH (8-11). This is collectively shown in given table.

**Table1:** The value of  $E_{pc}^1$  and  $I_{pc}^1$  from the cyclic voltammogram of Losartan potassium  $3 \times 10^{-3}$  mole /dm<sup>3</sup> in Robinson buffer (pH =8) used as supporting electrolytes with different scan rates at 30°C.

| 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                   |

**Table2:** The value of  $E_{pc}^2$  and  $I_{pc}^2$  from the cyclic voltammogram of Losartan potassium  $3 \times 10^{-3}$  mole /dm<sup>3</sup> in Robinson buffer (pH =8) used as supporting electrolytes with different scan rates at 30°C.

| Scan rates | $E_{pc}^2$ | $E_{p/2}$   | $E_{pc} - E_{p/2}$ | $\alpha = 48/E_{pc} - E_{p/2}$ | $I_{pc}^2 \times 10^6$ (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:** The value of  $E_p$  and  $I_p$  from the cyclic voltammogram of Losartan potassium  $3 \times 10^{-3}$  mole /dm<sup>3</sup> in Robinson buffer (pH = 11) used as supporting electrolytes with different scan rates at 30°C.

| S.No | Scan rate (mV/S) | Anodic peak    |                              | Cathodic peak  |                              |
|------|------------------|----------------|------------------------------|----------------|------------------------------|
|      |                  | $E_p$ (mV) -ve | $I_{pa} \times 10^{-6}$ (μA) | $E_p$ (mV) -ve | $I_{pc} \times 10^{-6}$ (μA) |
| 1    | 20               | 766.7±0.01     | 0.244±0.01                   | 798.4±0.02     | 1.330±0.01                   |
| 2    | 100              | 745.5±0.20     | 0.681±0.01                   | 802.4±0.02     | 1.806±0.015                  |
| 3    | 200              | 725.9±0.25     | 0.725±0.02                   | 821.9±0.3      | 2.744±0.02                   |
| 4    | 300              | 717.6±0.01     | 1.119±0.03                   | 823.0±0.03     | 3.944±0.02                   |
| 5    | 400              | 717.6±0.25     | 1.494±0.02                   | 823.0±0.15     | 4.163±0.01                   |
| 6    | 500              | 711.1±0.22     | 1.669±0.01                   | 827.8±0.15     | 5.052±0.01                   |

**Table 4:** The value of  $E_{pa/2}$  and  $E_{pc/2}$ , ( $\Delta E = E_{pa} - E_{pc}$ ) and  $I_{pa}/I_{pc}$  from the cyclic voltammogram of Losartan potassium  $3 \times 10^{-3}$  mole /dm<sup>3</sup> in Robinson buffer (pH = 11) used as supporting electrolytes with different scan rates at 30°C.

| S.No | Scan rate (mV/S) | $E_{pa/2}$ (mV) -ve | $E_{pc/2}$ (mV) -ve | $\Delta E = E_{pa} - E_{pc}$ (mV/S) | $I_{pa}/I_{pc}$ |
|------|------------------|---------------------|---------------------|-------------------------------------|-----------------|
| 1    | 20               | 383.35±0.01         | 399.2±0.01          | 22.7±0.01                           | 0.183±0.01      |
| 2    | 100              | 372.75±0.20         | 401.2±0.21          | 56.9±0.021                          | 0.377±0.02      |
| 3    | 200              | 362.95±0.012        | 410.9±0.021         | 95.1±0.021                          | 0.264±0.02      |
| 4    | 300              | 358.8±0.012         | 411.5±0.01          | 105.4±0.31                          | 0.284±0.21      |
| 5    | 400              | 356.1±0.3           | 411.5±0.01          | 105.4±0.15                          | 0.358±0.03      |
| 6    | 500              | 355.55±0.31         | 413.0±0.02          | 116.7±0.15                          | 0.330±0.031     |

**Table 5:** values of  $\alpha$ , Diffusion coefficient,  $R^2$  and Slope of  $I_{pc}^1$  of 3mM concentration of losartan potassium at different pH of buffer at 100mV/S.

| S.No | pH | $\alpha$    | "D" (cm <sup>2</sup> /s) 10 <sup>-6</sup> | Slope "m" 10 <sup>-6</sup> | $R^2$      |
|------|----|-------------|-------------------------------------------|----------------------------|------------|
| 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 |

**Table 6:** values of  $\alpha$ , Diffusion coefficient,  $R^2$  and Slope of  $I_{pc}^2$  of 3mM concentration of losartan potassium

| S.No | pH | $\alpha$    | "D <sup>1/2</sup> " (cm <sup>2</sup> /s) 10 <sup>6</sup> | Slope "m" 10 <sup>-6</sup> | $R^2$      |
|------|----|-------------|----------------------------------------------------------|----------------------------|------------|
| 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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