Cyclic voltammetric studies of Gemifloxacin using Gold electrode in presence of Britton-Robinson Buffer

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Abstract: The electrochemical study of the Gemifloxacin has been conducted using cyclic voltammetry technique at gold electrode. Gemifloxacin is antibacterial compound. In present study the electrochemical parameters of Gemifloxacin were determined in (0.04M) Britton Robinson Buffer as a supporting electrolyte at different pH ranging from 2-6 pH. This buffer was selected according to the appropriate solubility of these pharmaceutical compounds. Voltammograms of Gemifloxacin have been recorded at six different scan rates of 20, 100, 200, 300, 400 and 500mV/s. Different electrochemical parameters such as peak potential (E_p), peak current (I_p), transfer coefficient (α), number of electron (n_α), diffusion coefficient (D), and heterogeneous rate constant (K^0) were determined. Moreover, diagnostics tests have also been applied to define the electrochemical behavior of Gemifloxacin showed quasi reversible redox process with two electron transfers at the electrode.

Keyword: Gemifloxacin, cyclic voltammetry, gold electrode, antibacterial compound, electrochemical parameters, Britton Robinson buffer, supporting electrolyte, quasi reversible, adsorption.

INTRODUCTION

Gemifloxacin is biologically active compound is a yellow, crystalline powder and soluble in water with a molecular mass 389.381gm. The I.UP.A.C name of Gemifloxacin (GFX) is [(R, S)-7-[4Z)-3-(aminomethyl)-4-(methoxyimino)-1-pyrolidinyl]-1-Cyclopropyl-6-fluoro-1,4 dihydro-4-oxo-1,8-napthyridin-3-carboxalic acid mesylate (Al-Mohaimeed *et al*., 2012;Anapathy *et al*., 2009; Ebraheem *et al*.,2011, Madhuri *et al*., 2010[a]; Madhuri *et al*., 2010[b]; Radi *et al*.,2013;Sahu *et al*., 2012; Wahed http://www.hindawi.com/38701068/*et al*.,2014;)

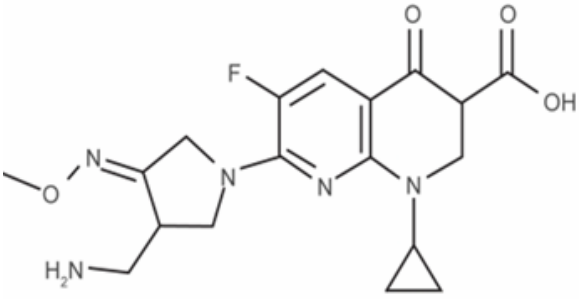

Fig. 1: Structure of Gemifloxacin

Gemifloxacin (GFX) is a kind of flouroquinolone which belongs to the class of antibacterial drugs (Anapathy *et al*., 2009; Madhuri *et al*., 2010[a], Madhuri D *et al*., 2010[b]; Mohammad *et al*., 2010; Oh *et al*., 1996; Sultana *et al*., 2011).With enhanced affinity towards bacterial isomerase IV (Madhuri *et al*., 2010[a]; Radi *et al*., 2013; Sultana *et al*., 2011). After the approval of FDA (Food drug administration) of infections of the respiratory and genitourinary (Al-Mohaimeed *et al*., 2012; Blondeau and Tillotson, 2007). GFX can also be used for (Radi *et al*., 2013; Öncü 2007).Treatment of pneumonia and acute bacterial exacerbation of chronic bronchitis (Al-Mohaimeed *et al*., 2012; Ebraheem *et al*., 2011; Mohammad *et al*., 2010; Sahu *et al*., 2012; Radi *et al*., 2013). This compound has a wide-range of therapeutic effect against gram positive and gram negative bacteria (Ellie and Goldstein., 2000; Oh *et al*., 1996; Öncü., 2007; Radi *et al*., 2013). It is in particularly active against penicillin microlide and quinolone resistant streptococcus pneumonia (Ellie and Goldstein, 2000; Sultana *et al*., 2011). Moreover, GFX has also potent activity against the other major pathogens involved in respiratory tract infections including haemophilus, influenza, and moraxella and catarrhalus (Al-Mohaimeed *et al*., 2012; Wahed *et al*., http://www.hindawi.com/38701068/2014). However, it is also used for treatment of urinary tract infection and bronchitis (Kadi *et al*., 2013; Madhuri *et al*., 2010[b]).Literature Review reveals that the pharmacological and other analytical aspects of Gemifloxacin (GFX) have been studied by various analytical methods. These include high performance chromatography (Kim *et al*., 2004; Narayan *et al*., 2014); liquid chromatography resolution microchip electrophoresis method (Cho *et al*., 2004;Kim *et al*., 2004). Tandem mass spectroscopy (LC-MS/ MS) (Kadi *et al*., 2013). Different spectrophotometric methods (Anapathy *et al*., 2009; Ebraheem *et al*., 2011; Gouda *et al*., 2014; Krishna *et al*., 2008; Madhuri *et al* 2010[a]; Madhuri *et al* 2010[b]; Naveed *et al*., 2015; Sahu *et al*., 2012; Wahed *et al*., 2014); and reversed phase chromatography (Mohammad *et al*., 2010; (Rote and

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Pingle, 2009. A fluorometric method (Atia *et al*., http: //www.hindawi.com/10591547/2013; *Tekkeli* and Önal, 2011)*;* was also reported for the determination of GFX in plasma, simultaneous determination of GFX and diuretics in bulk and in human serum by RP-HPLC (Sultana *et al*., 2011). Recently, volatmmetric determination using screen print carbon, sensor/biosensor electrode (Al-Mohaimeed *et al.,* 2012; Radi *et al* 2013); and multi wall carbon nanotubes modified glassy carbon electrode have also been used to explain the pharmaceutical, electrochemical and biological role of GFX (Jain and Rather, 2011).

In the present study the quantitative and qualitative investigations of Gemifloxacin were carried out by cyclic voltammetry technique at gold electrode. In this technique current flow between the working electrode and a counter electrode is measured under the control of a potentiostate. The voltammogram is recoded on a recorder which determines the peak potentials (E_p) and peak current density (I_P) (Bard and Faulkner, 2001; Bockris *at el*., 2006). The result gives sufficient information about the thermodynamics of redox reaction, kinetics of heterogeneous electron-transfer reactions, adsorption or diffusion processes and coupled chemical reactions (Greef *et al.,* 1985). Moreover, this technique can also be used for quality control and pharmacokinetics studies of biologically active compound.

MATERIALS AND METHODS

Reagents

A Stock solution of Gemifloxacin ($3x10^{-3}$ mole/dm^3) was prepared in 0.04M Britton Robinson Buffer (B-R). This B-R buffer was prepared in laboratory which was used as supporting electrolyte. All other reagents were analytical grade and prepared in double distilled water during the experiment.

Instrumentation

This experiment was performed with CHI- 700c and three different electrodes system, a Gold test electrode was used as working electrode, a Hg/Hg_2Cl_2 electrode as reference electrode and platinum wire (Pt) as counter electrode. A pH- meter (Jenvay–3510) and conductivity meter (Romania) HANNA (HI-8633) were also used for monitoring the pH and conductivity of the electrolytic system throughout the experiment.

General Procedure

Before taking the voltammogram of the Gemifloxacin recorded the base line. Base line of supporting electrolyte was found to be straight at potential window (0 to –0.6 V) and after that the electrochemical cell was filled with 10 ml solution of Gemifloxacin (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 20min to avoid oxygen interference. The voltammograms of the analyte were recorded at 30±1ºC on computer. During the experiment surface of gold electrode was renewed time to time by polishing with alumina and washing with distilled water (Inc. Manual. CHI700c).

Volt ammogram were recorded the six different scan rates (υ) (20, 100,200,300,400.500) mV/sec) while the potential range was adjusted from 0 to –0.6 V.

RESULTS

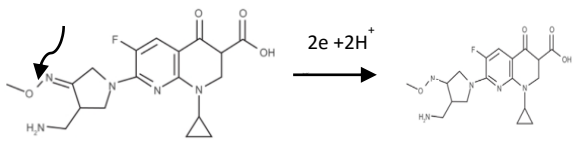
In this research work study the electrochemical behavior of Gemifloxacin showed quasi reversible redox process with two (2) electron transfer as well as some adsorption complications has been observed. Furthermore, different parameters such as peak potential (E_p), half peak potential ($E_{p1/2}$), peak current (I_p) transfer coefficient (α) was found within the range. Ratio of I_{pa}/I_{pc} approximately ≈ 1. However, values of diffusion coefficient (D) was observed with in limit $10^{-6}cm^2/S$, and heterogeneous rate constant (K^0) was found within range reported in literature. However drastic change was observed E^0 vs. pH. Proposed reaction mechanism was also described which may occur with the transfer of two electron or two protons.

DISCUSSION

The CV profiles of Gemifloxacin showed two cathodic peaks and one revese andoic weak peak at potential range of 1.0 to - 0.8V in B-R buffer (fig. 1). The Values of electrochemical parameters inferred from the literture at different scan rates are given in (table 1).

Proposed reaction mechanism

As the cyclic voltammograms of Gemifloxacin exhibit the reduction process by showing two well defined cathodic peaks and one broad anodic peak which may occur with the transfer of two electrons and two protons. The most susceptible position for reduction process is –O−N group as represented in (scheme 1) above mentioned proposed reaction mechanism of Gemifloxacin.



Scheme 1: Proposed reaction mechanism.

Effect of scan rate

The peak current (I_p) increased with increase of scan rates. Moreover, the plot of peak current ($I_{pc}{}^1$), and ($Ip_a{}^1$) vs. square root of scan rate ($\upsilon^{1/2}$) showed linear relationship but not proportional to $\upsilon^{1/2}$ (fig. 2). Moreover,

the peak current I_{pc}^1, I_{pc}^2 and I_{pa}^1 verus square root of the potential scan rates ($\upsilon^{1/2}$) gives slope values less than theoretical value 0.5 for diffused species which is shown in (fig. 3). It indicates that the electrode surface has some adsorption complications (Ali and Sami, 2000; Hegde *et al*., 2008).

Effect of pH

The voltammogram of Gemifloxacin clearly showed two cathodic peaks and one anodic peak at pH 2.-3. However, at pH 4 and 5 the andodic peak was gradually suppressed and at pH 6 it was completely disappered (fig. 4). Moreover, an increase in the peak current (I_p) and was also observed with the increase in the pH. Therefore, it can be concluded that pH may affect solublity of compound and the electrochemical process particularly oxidation process (Tesfaw, 2010).

The value of n was estimated by using formal potential (E^0) was determined by the midpoint potential (Emid) between the E_{pa}^1 and E_{pc}^1 (Tesfaw, 2010). The E^0 then plotted as a function of pH of the solution (fig. 5) (Malode and Nandibewoor, 2013).

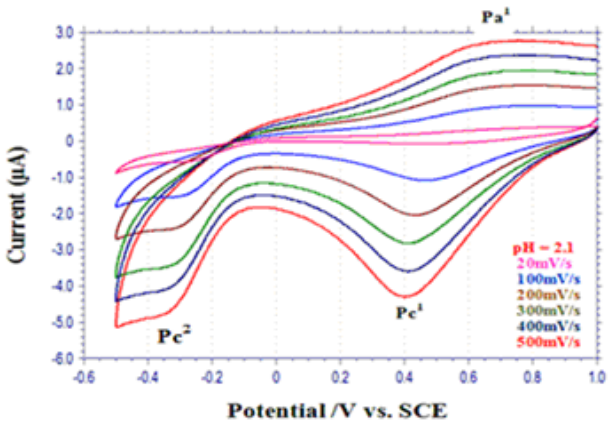


Fig. 1: Cyclic voltammograms of 3mM Gemifloxacin with different scan rates in the presence of 0.04M B-R buffer (pH=2.1) at gold electrode vs. SCE reference electrode at 30±1ºC.

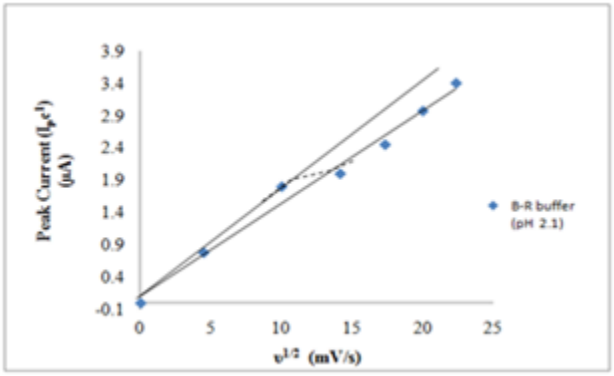


Fig. 2: Plot of I_{pc}^1 vs. $u^{1/2}$ of 3mM Gemifloxacin in the presence of 0.04 M R-B buffer (pH=2.1) at 30±1ºC.

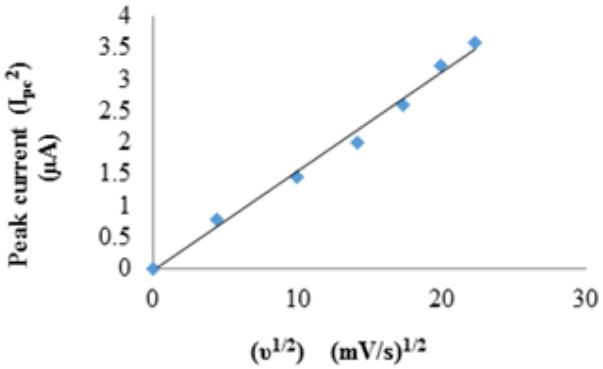


Fig. 3: Plot of I_{pc}^2 vs. $u^{1/2}$ of 3mM Gemifloxacin in the presence of 0.04 M R-B buffer (pH=2.1) at 30±1ºC.

E^o = -0.310 pH + 6.250 (R^2=0.71) (1)

$E^0 = E^0_{pH=0} -$ (2.303mRT/2F) pH where m is number of protons = number of electron (Hassan *et al*., 2015; Malode and Nandibewoor, 2013. Thus, n=1.04 E_1 at first peak.

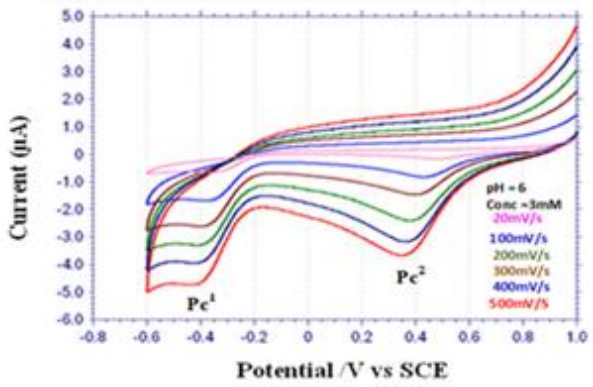


Fig. 4: Cyclic voltammograms of 3mM Gemifloxacin with different scan rates in the presence of 0.04M B-R buffer (pH=6) at gold electrode vs. SCE reference electrode at 30±1ºC.

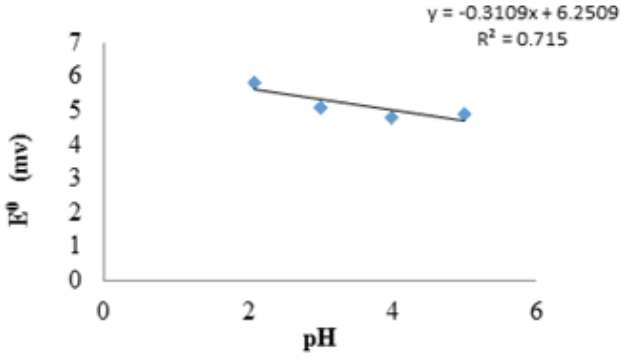


Fig. 5: Plot of E^0 vs. pH of (3mM) Gemifloxacin in the presence of (0.04 M) B-R buffer with 100mV/s rate at 30±1ºC.

The second cathodic peak showed no corresponding anodic peak and the number of electron (n=1.2~1) was

estimated by using the value of αn (0.90) which was estimated by using slope (0.06) of E_{pc}^2 versus log υ shown in (fig. 6) while value of α (0.6) calculated by using equation (2) which was used to estimate the number of electron transferred for second cathodic peak (Greef *et al*., 1985).

$$\alpha = 47.7/ Epc- - Ep_{/2} \quad (2)$$

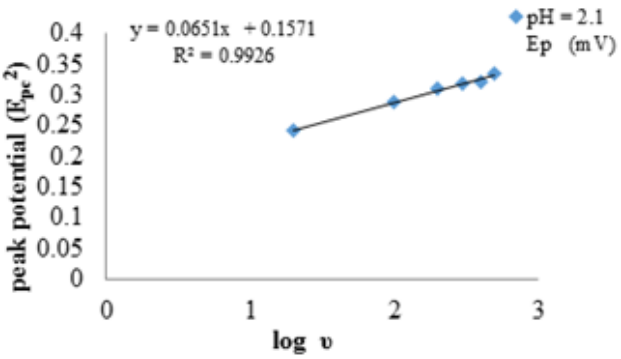


Fig. 6: Plot of E_{pc} vs. log of u of (3mM) Gemifloxacin in the presence of 0.04M B-R (pH=2.1) buffer at 30±1ºC.

Effect of concentraction

A linear dependence of peak current (I_{pc}) on the concentraction (1×10^{-3}-3×10^{-3}M) of Gemifloxacin was observed in B-R buffer (fig. 7). This linear behaviour suggests the diffusion is the rate limiting process (Ali and Sami, 2000; Greef *et al*., 1985; Hassan *et al.*, 2015).

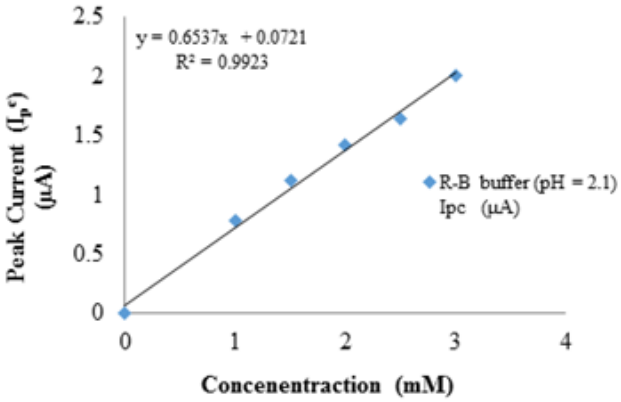


Fig. 7: Plot of 1_{pc} vs. different concentration (1mM-3mM) of Gemifloxacin with 100mV/s rate in the presence of 0.04 M B-R buffer (pH=2.1) at 30±1ºC.

Heterogenous rate constant

The heterogeneous rate constant K^0 was obtained using the methodology described by Nicholson (Ali and Hassan, 2014; Brett and Brett, 1993, Hassan *at el*., 2015). Through a working curve between n (ΔE_p^c-E_p^a) and Ψ the dimensionless kinetic parameter, Ψ were obtained by using a linearization of the Nicholson approach. Finally, the obtained Ψ value and other parameters which were previously described were used to calculate K^0 which are represented in (table 2).

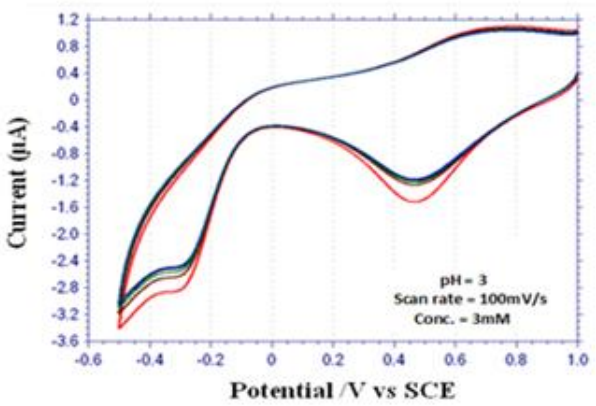


Fig. 8: Repeated cyclic voltammograms of 3mM Gemifloxacin at gold electrode vs. SCE reference electrode with 100mV/s scan rate in the presence of 0.04 M B-R buffer (3=pH) at 30±1ºC.

$$K^0 = \Psi \left(\pi Do \frac{nF}{2RT}\right)^{1/2} \quad (3)$$

The repeated cyclic voltammogram

The repeated cyclic voltammograms of Gemifloxacin were recorded at (100mV/s) scan rate in the presence of supporting electolyte (fig. 8). The decrease in peak current (I_p) has been observed as a result of sucessive cycling. The descreased peak current (I_p) indicates a slow or weak adsorption of the analyte at gold test electrode which is as reported in literature (Ali and Hassan, 2014; Hassan *at el* 2015, Ali and Sami, 2000; Greef *et al*., 1985).

Diagonestic test for quasi reversibile

The recorded voltammograms of Gemifloxacin demonstrating the redox process by showing one reverse anodic peak and two cathodic peaks (fig. 1). The second cathodic peak (I_{pc}^2) shows irreversibility while the first cathodic peak (I_{pc}^1) and its corresponding anodic peak (I_{pa}^1) indicates quasi reversibility. The estimated parameters for Gemifloxacin also show the quasi reversible process by follwing the diagonstic certeria (table 3) (Ali and Hassan, 2014; Brett and Brett, 1993, Hassan *et al*., 2015).

1. Increase in Ip^a with $\upsilon^{1/2}$ but not propotional to it.
2. $|I_{pa}/ I_{pc}| = 1$ provided $a_c = a_a = 0.5$
3. Shifting of E_p^c negatively with increasing scan rate
4. ΔE_p is greater than 59/nmV and increases with υ

CONCLUSION

The investigation of electrochemical properties of GMX has been carried out by cyclic voltammetery technique to examine different parameters such as peak current(I_p), peak potential (E_p), Diffusion coefficient (D), transfer coefficient (α) which are used to reveal the nature of electrochemical process, number of electron transferred (n) and type of electrode reactions.

Table 1: The values of E_{pc}^1,I_{pc}^1, $E_{p1/2}$, (E_{pc}^1 -$E_{p1/2}$) , E_{pc}^2,I_{pc}^2 $E_{p1/2}$, (E_{pc}^2 -$E_{p1/2}$) ,and E_{pa},I_{pa}, $E_{p1/2}$, (E_{pa} -$E_{p1/2}$),(α) and (D) from the cyclic voltammograms of 3mM Gemifloxacin in the presence of 0.04M B-R buffer (pH = 2.1) with different scan rates at 30±1ºC.

S. No.	Scan rate (mV/s)	pH = 2.1					
		First Peak (Cathodic)					
		E_{pc}^1 (mV)	I_{pc}^1 (µA)	$E_{p1/2}$ (mV)	E_{pc}- $E_{p1/2}$ (mV)	[a]α	[b]D×10^6(cm^2/s)
1	20	546 ± 24	0.8±0.1	465±24	81± 15	0.6± 0.1	1.5±0.1
2	100	515 ± 35	1.8±0.1	595±35	80±25	0.6±0.1	1.6±0.1
3	200	503 ± 27	2.0±0.12	590±28	82±26	0.6±0.1	1.0±0.2
4	300	433 ± 34	2.5±1.8	529±32	96±21	0.5±0.2	1.0±0.2
5	400	409 ± 20	3.0±2.1	515±25	96±38	0.5±0.2	0.8±0.3
6	500	405 ± 19	3.4±1.8	510±23	95±22	0.5±0.1	0.8±0.2
S. No.	Scan rate (mV/s)	pH = 2.1					
		Second Peak(Cathodic)					
		E_{pc}^2 (mV)	I_{pc}^2 (µA)	$E_{p1/2}$ (mV)	E_{pc}- $E_{p1/2}$ (mV)	[a]α	[b]D×10^6 (cm^2/s)
1	20	299±25	0.64±0.1	250±15	50± 15	0.9± 0.1	0.98±0.02
2	100	321±20	1.5±0.1	258±10	62±15	0.7±0.1	0.84±0.11
3	200	331±25	2.0±0.2	266±12	65±26	0.7±0.1	0.83±0.21
4	300	344±18	2.3±0.1	265±17	79±21	0.6±0.3	0.67±0.21
5	400	347±31	2.6±0.2	278±18	68±27	0.7±0.2	0.65±0.31
6	500	362±19	2.98±0.3	286±19	75±27	0.6±0.1	0.694±0.25
S. No.	Scan rate (mV/s)	pH = 2.1					
		Third Peak (Anodic)					
		E_{pc}^2 (mV)	I_{pc}^2 (µA)	$E_{p1/2}$ (mV)	E_{pc}- $E_{p1/2}$ (mV)	[a]α	[b]D×10^6 (cm^2/s)
1	20	634± 30	0.7±0.1	555±20	79± 15	0.6± 0.1	1.5±0.2
2	100	650 ± 25	1.7±0.1	570±15	80±12	0.6±0.3	1.4±0.1
3	200	679 ± 17	2.0±0.6	590±8	89±06	0.6±0.1	1.0±0.2
4	300	703 ± 14	2.5±1.8	605±31	98±21	0.5±0.2	1.0±0.2
5	400	708 ± 18	3.0±2.1	610±10	98±18	0.5±0.2	1.1±0.3
6	500	711 ± 26	3.6±1.8	617±18	99±12	0.5±0.1	0.9±0.2

a) α = 47.7/ Epc- - Ep/2

b) I_p = - (2.6 × 10^5) $n^{3/2}$C A$D^{1/2}$$\upsilon^{1/2}$(Randles Sevick equation is used to calculate the "D

Table 2: **T**he values of n (E_{pa}-E_{pc}), Ψ and heterogeneous rate constant at 100mV/s scan rate.

S. No.	pH	n(E_{pa}-E_{pc}) mV/s)	Ψ	First Cathodic peak (K^0) (cms^{-1})	First anodic peak (K^0) (cms^{-1})
1	2	135	0.5	9.5×10^{-3}	9.2×10^{-3}
2	3	176	0.25	4.62×10^{-3}	4.09×10^{-3}
3	4	155	0.4	5.96×10^{-3}	7.9×10^{-3}
4	5	-	-	-	-
5	6	-	-	-	-

Table 3: The values of (α), (I_{pa}/I_{pc}) and ΔE from the cyclic voltammograms of 3mM Gemifloxacin in the presence of B-R buffer (pH = 3) with different scan rate at 30±1ºC.

S. No.	Scan rate (mV/s)	α	I_{pa}/I_{pc} (µA)	ΔE (mV/s)
1	20	0.60	0.98	115
2	100	0.59	0.98	176
3	200	0.56	1.04	205
4	300	0.56	0.98	222
5	400	0.56	0.94	235
6	500	0.56	0.90	255

The drug Gemifloxacin, represented quasi reversible reaction behavior by following the maximum criteria of quasi reversible diagnostics test. It showed adsorption controlled process on surface of the test electrode and involvement of pH and concentration in the present electrochemical process.

These parameters determined in this study by CV technique would be helpful for formulation or evaluation drug dosage with the consideration of physio-chemical parameters such as pH and concentration. This method is suitable for quality control laboratories as well as pharmacokinetic studies. Moreover, this technique is suitable alternative due to easy handling and less time consuming as compared to other techniques such as HPLC or chromatography.

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