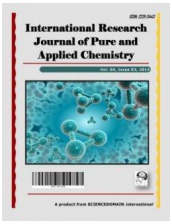

International Research Journal of Pure & Applied Chemistry
8(4): 221-228, 2015, Article no.IRJPAC.2015.087
ISSN: 2231-3443

SCIENCEDOMAIN *international*
www.sciencedomain.org

Cyclic Voltammetric Study of Clarithromycin Using Gold Electrode

Atya Hassan[1*], S. Azhar Ali[2] and Mahboob Muhammad[3]

[1]Department of Chemistry, Federal Urdu University of Arts, Science and Technology, Gulshan Iqbal Campus Karachi, Karachi, Pakistan.
[2]Department of Chemistry, University of Karachi, Karachi, Pakistan 7520, Pakistan.
[3]International Center for Chemical and Biological Sciences, H.E.J. Research Instiute of Chemistry, University of Karachi, Karachi, Pakistan.

Authors' contributions

This research work was carried out in collaboration between all authors. Author SAA designed this project. Author AH preformed this experimental analysis, managed the literature search and wrote this manuscript with assistance from author SAA. Author MM provided the instrumental facilities. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IRJPAC/2015/18141
Editor(s):
(1) Wolfgang Linert, Institute of Applied Synthetic Chemistry Vienna University of Technology Getreidemarkt, Austria.
Reviewers:
(1) Anonymous, Indiana University, USA.
(2) Anonymous, Federal University of Technology, Nigeria.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=1052&id=7&aid=9560

Original Research Article

Received 7th April 2015
Accepted 6th May 2015
Published 2nd June 2015

ABSTRACT

Clarithromycin is biologically active compound which is belonging to the class of antifungal compound. This is used for the treatment of HIV patients. In present study the electrochemical parameters of clarithromycin has been carried out through cyclic voltammetry technique. These parameters have been studied in presence of Briton Robinson buffer pH range (2-6) has been selected according to the appropriate solubility of clarithromycin. Voltammograms of the clarithromycin have been recorded at six different scan rates of 20, 100, 200, 300, 400 and 500mV/s. Different electrochemical parameters such as peak potential (Ep), peak current (Ip), transfer coefficient (α), number of electron (nα), diffusion coefficient (D), and heterogeneous rate constant (K0) were determined. Moreover, diagnostics tests have also been applied to define the electrochemical properties of these compounds. In case of Clarithromycin irreversible oxidation

**Corresponding author: E-mail: atya007chem@yahoo.com;*

process with two electron transfer has been identified and electrode processes were shown to be diffusion controlled.

Keywords: Clarithromycin; biologically active; antifungal; treatment of HIV; cyclic voltammetry; electrochemical parameters.

1. INTRODUCTION

Clarithromycin (CAM) is semi synthetic antimicrobial 14–membered macrolide compound exhibiting a broad in vitro antibacterial spectrum [1]. It is a white crystalline solid and partially soluble in water. Its molecular formula is $C_{38}H_{69}NO_{13}$ and molecular weight is 747.96 gm. Molecular Structure of CAM shown in (Fig. 1). Its common name is Clarithromycin (CAM). Its IUPAC name is (3R, 4S, 5S, 6R, 7R, 9R, 11S, 12R, 13S, 1S)-6-{[(2S, 3R, 4S, 6R) -4-(dimethylamino)-3hydroxy-6-methyloxan-2-yl]oxy}-14ethyl, 12, 13dihydroxy-4{[(2R, 4S, 5S, 6S)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yi]oxy}-7-methoxy-3,5,7,9,11,13-hexamethyi-1-oxacyclotetradeceane,10 di-one [2].

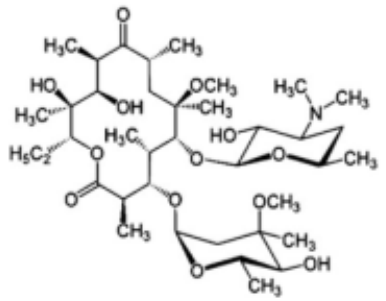

Fig. 1. Structure of clarithromycin

Clarithromycin (CAM) is partially synthetic macrolide antibiotic [1-3]. It has good stability in gastric acid and isolated from erythromycin [4]. It acts as anti-infective, gastrointestinal and antibacterial agent. Recently, it is commonly used for therapy [5] with various clinical benefits such as better oral bioavailability, with broad spectrum activity, higher tissue concentration and improved tolerability. The combining effect of Clarithromycin with a variety of other drugs for the treatment and preventation of disseminated mycobectrium avium-intracellular complex (MAC) infection in patients with Immune deficiency syndrome (AIDS) is also under investigation [6-8].

Reported investigations have indicated that variety of techniques related to qualitative and quantitative determination of Clarithromycin (CAM) has been used. For instance UV-spectroscopy [9-11], electrochemical methods [12,13], sensitive liquid chromatography (SLC) technique were used for the analysis of Clarithromycin (CAM) in human serum [14]. In addition, high performance liquid chromatography (HPLC) with electrochemical detection (ED) has also been applied for CAM. Recently determination of electrochemical behavior of Clarithromycin by single- sweep oscillopolarography [15] and electrochemical activity of (CAM) were reported at gold electrode with 0.05 M $NaHCO_3$ [16].

Aim of this work is to focus on the application of cyclic voltammetry technique for the determination of electrochemical parameters such as peak potential ($E_{p)}$,half peak potential ($E_{p1/2}$), Peak Current (I_p), transfer coefficient (α), diffusion coefficient (D), number of electron transfer (n) and heterogeneous rate constant (K°) and chemical nature of different biologically active drugs [17-21]. For the electrochemical investigation of biologically active compound, gold as test electrode has been selected to understand its applicability as non toxic test electrode as compared to the other mostly used electrodes like a Hg dropping electrode and carbon paste electrode. These investigations would also be helpful to evaluate the pharmacological effect of other different biologically active compounds in vivo and vitro studies.

2. MATERIALS AND METHODS

2.1 Experimental

Analytical grade reagents were used in present research work. A stock solution of Clarithromycin (4 mM) was prepared by dissolving 0.298 gm in 100 ml volumetric flask which was filled with B-R buffer (used as supporting electrolyte) at 30±1°C. Same procedure was repeated for the preparation of the solution with different pH of the B-R-buffer solutions.

2.2 Instrumentation

Recently, 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. The Cyclic Voltammetry (CHI-700c) with three different electrodes system, a gold electrode was used as working, a calomel electrode (Hg/Hg_2Cl_2) as reference and platinum wire (Pt) as counter electrode respectively.

2.3 Determination of Cyclic Voltammogram of Sample

Residual or back ground currents were estimated in the determination of base line in each supporting electrolyte to minimize the effect of non faradic contribution in total current. This was done before each cyclic voltammogram taken either in quantitative or qualitative studies. After recording the base line in B-R buffer used as supporting electrolyte, the electrochemical cell assembly was rinsed thrice with the solution of these analyte being prepared in the same supporting electrolyte. After this 10 cm^3 of analyte was transferred to the cell and ensured the removal of air bubble (argon (99.99%) gas was purged for 20 minutes to have inert atmosphere) from the surface of gold electrode and adjusted the electrode assembly in the cell. This procedure was similar as followed for the base line determination. Voltammograms were recorded at different scan rates like 20, 100, 200, 300, 400 and 500 mV/s. Same procedure was repeated with other biological active compounds.

3. RESULTS AND DISCUSSION

In the present study electrochemical behavior of Clarithromycin was examined by using B-R buffer as supporting electrolyte within the range of pH 2-6. The cyclic voltammograms of Clarithromycin (3mM) were recorded at gold test electrode between the ranges of the (0 to +1.6V) potential window and scan rates were (20, 100, 200, 300, 400 and 500 mV/s).

The voltammogram of Clarithromycin represents one cathodic peak and two anodic peaks. (Fig. 2). The anodic peaks were observed in potential range of 1.0- 1.6 V/s and cathodic peak was appeared in the range of 0.2-0.6 V/s. In previous liteturer showed that cathodic peak in this range of potiential has also been reported due to reduction of gold electdrode surface [22,23]. Therefore, it can be concluded that the Clarithromycin undergoes irreversible oxidation and as result anodic peak appeared, while the observed cathodic peak is due to reduction of gold electrode surface which was confirm with blank shown in (Fig. 3).

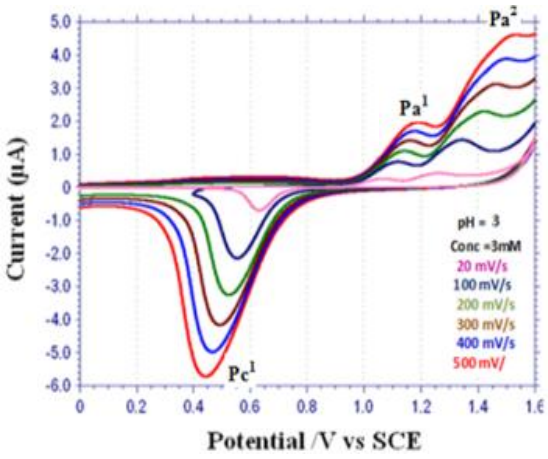

Fig. 2. Cyclic voltammograms of 3 mM Clarithromycin with different scan rates in the presence of 0.04 M B-R buffers (pH= 3.0) at gold electrode vs. SCE reference electrode at 30±1°C

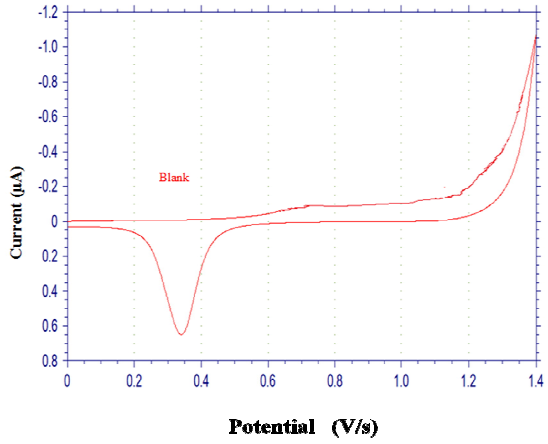

Fig. 3. Cyclic voltammograms of 0.04 M B-R buffers at gold electrode vs. SCE reference electrode with 100 mV/s at 30±1°C

3.1 Stuggested Reaction Mechanism

As the voltammogram of Clarithromycin showed two anodic peak (Fig. 4) which indicate the occurrence of oxidation process most prbably to the two exposed OH- groups as shown in structure of Clarithromycin. Due to the removal of hydrogen, “OH” groups have been oxidized and negative charged has appeared as O- after the oxidation in Clarthromycin.

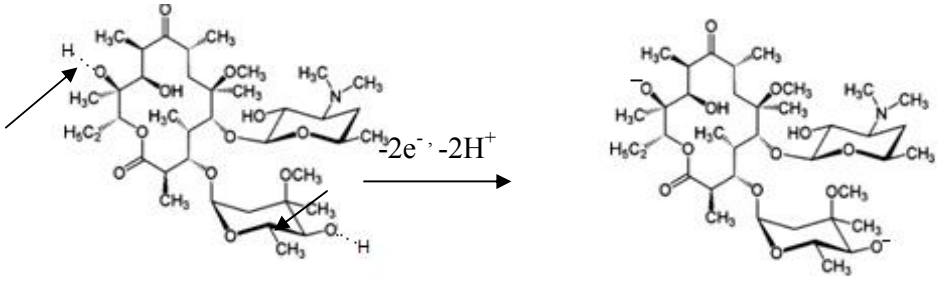

Fig. 4. Suggested Reaction mechanism

3.2 Digonestic Criteria for Irreversible System

To verify the irrversible transfer mechanism, diagonistic test for irrversibility has also been applied. Clarithromycin showed peak current is propotional to the square root of scan rate. (Fig. 5) and Epc shifts $-30/\alpha_C n_\alpha$ mV for each decade increase in scan rate (υ) as describe the third criteria of irreversibility while the difference of E_p- $E_{p/2}$ is against the reported criterion for total irreversibility [24,25] and it varies from 20 to 500 mV. However, by following the maximum point of irreversible diagnostic test, the electro oxidation process of Clarithromycin considered as irreversible.

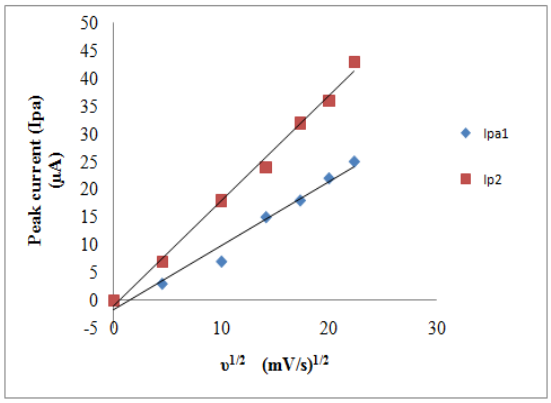

Fig. 5. Plot of I_p vs. $\upsilon^{1/2}$ of 3mM Clarithromycin in the presence of 0.04M R-B buffer (pH = 3.0) at 30±1°C

3.3 Effect of Scan Rate

The Effect of scan rate (υ) on peak current (I_{pa}^1 and I_{pa}^2) has also been studies for Clarithromycin. The plot of peak current I_{pa}^1(R^2=0.99) and and I_{pa}^2 (R^2=0.99) showed strong correlation with square root of scan rates ($\upsilon^{1/2}$) as shown in (Fig. 3). The plot of log of peak current I_{pa}^1 and, I_{pa}^2 verus log of scan rates (log υ) gives slope values 0.55 and 0.57 respectivly, which closed to the theoritical value 0.5 for diffusion controlled process rather than adsorption [23].

The peak potientials (E_{pa}^1 and E_{pa}^2) were showed linear corelation with log of scan rates (log υ) as shown in (Fig. 6) and this behaviour was consistent with electrochemical nature of the reaction in which electrode reaction is coupled with an irrversible follow- up chemical step [22].

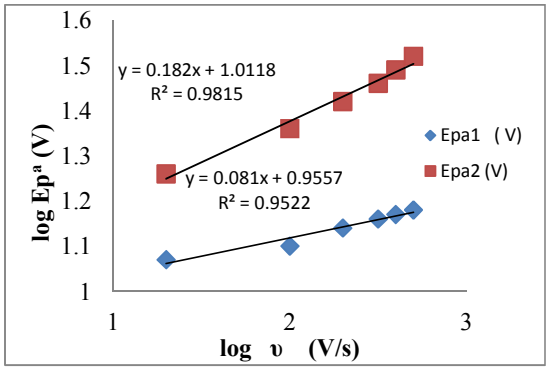

Fig. 6. Variation in log Ep^{a1} and log Ip^{a2} vs. Logυ of 3 mM Clarithromycin in 0.04 M B-R buffer

The linear relation between E_{pa} and log of scan rate (log υ) can be represented by following equations.

$$E_p^{a1} = 0.182\log\upsilon + 1.011 \quad (1)$$
$$E_p^{a2} = 0.085\ \log\upsilon + 0.949$$

In case of irrversible process (E_p) peak potiential is defined by Laviron and expressed in equation (1).

The values of α n was calculated from slope values of E_p vs log υ. Slope of first plot slope is 0.18 and α n is 1.08 and for second plot is 0.08, therefore α n is 1.07. Moreover, the value of α

was calculated according to Bard and Faulkner by using (2). The value of α (0.71) and α (0.6) for first peak and second peak respectively. Thus, the number of electron for first peak is 1.4~1 and for second peak 1.3~1 have been observed which showed the transfer of two electrons in electro oxidation process of the Clarithromycin.

$$\alpha = \frac{47.7}{Ep - Ep/2}\,mV \qquad (2)$$

3.4 Effect of pH

The voltammograms of Clarithromycin at different pH showed variations in anodic peak. At pH (2.5, 3 and 3.5) two andodic peak were noted (Fig. 2). At pH 4 and pH 5 only one anodic peak have been observed (Fig. 7). This variablity in peaks and peak currents (Fig. 8) shows the solublity of Clarithromycin is affacted by the pH and as result variation in voltammogramms have been observed.

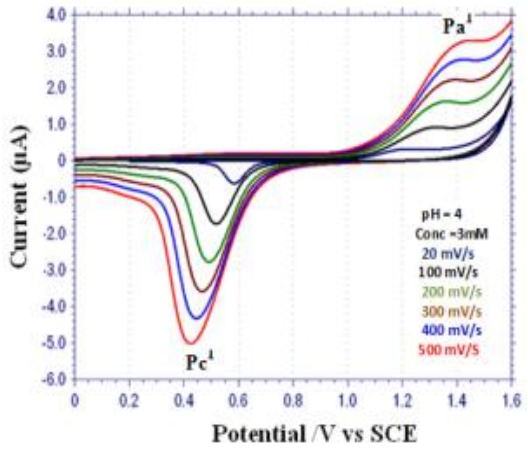

Fig. 7. Cyclic voltammograms of 3 mM clarithromycin with different scan rates in the presence of 0.04 M B-R buffers (pH= 4.0) at gold electrode vs. SCE reference electrode at 30±1°C

3.5 Effect of Concentraction

The peak current (I_p^a) was directly proportional to concentration of analyte (1×10^{-3}- 3×10^{-3} M) at pH 2.5 (Fig. 9). This linear dependence of peak current (I_p^a) on concentraction of Clarithromycin represents diffusion as rate limiting step as explained by the A. Bard and Faulkner [26].

3.6 Transffer Coefficents

The values of charge transfer cofficients (α) were calculated by using the value of the potential difference E_p-$E_{p1/2}$ as described before [24,25]. This charge transfer coefficients is given in (Table 1), lies within the range of 0.5 to 1 as defined for totally irreversible reaction . The value of (α) is also dependent on the potential difference $|E_p$-$E_{p1/2}|$ in case of irreversible systems.

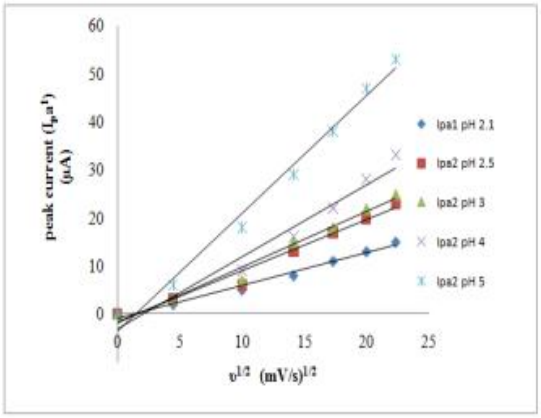

Fig. 8. Effect of pH on peak current of 3mM clarithromycin (I_{pa} vs. $\upsilon^{1/2}$) with different scan rates at 30±1°C

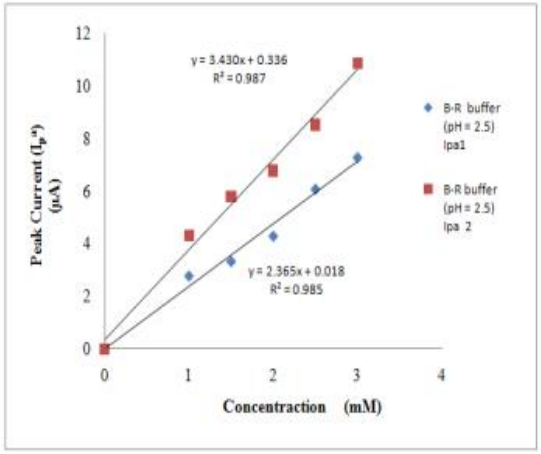

Fig. 9. Plot of I_{pa} vs. concentration (1 mM – 3 mM) of clarithromycin at 100 mV/s in the presence of 0.04M B -R buffer (pH=2.5) at 30±1°C

3.7 Heterogenous Rate Constant

The values heterogeneous rate constant of (k^0) was determined by using the value of E^0. The

value of E^0 were obtained from the intercept of E_p versus υ curve by extrapolating to the vertical axis at υ = 0 [23]. Reinmuth reported an alternative simple expression shown in given equation.

$$\frac{Ip}{nFA} = C_o K^0 \quad (3)$$

The value of heterogenous rate constant for Clarithromycin were shown in (Table 2).

3.8 The Repeated Cyclic Voltammogram

A gradual decrease in peak height (current) (Ip^c) as a result of repeated voltammograms at 100 mV/s in R-B buffer (Fig. 10) indicates slow or weak adsorption or desorption of analyte at gold test electrode as reported in literature [27].

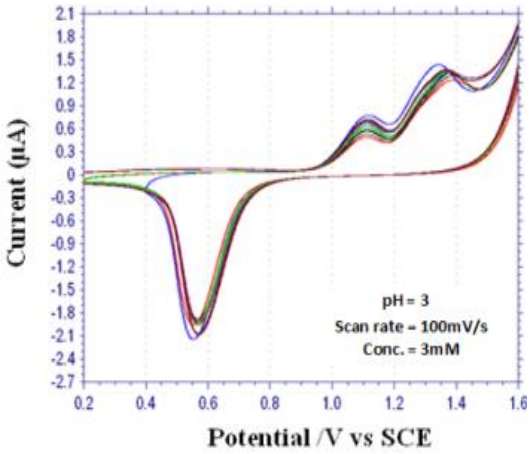

Fig. 10. Repeated cyclic voltammograms of 3 mM Clarithromycin at gold electrode vs. SCE reference electrode with 100 mV/s scan rate in the presence of 0.04 M B-R buffer (pH =3) at 30±1°C

Table 1. The values of peak potential (E_p), Peak current (I_p), Half peak potential ($E_{p1/2}$), Difference of peak potential and half peak potential (E_{pa}- $E_{p1/2}$), Transfer coefficient (α) and Diffusion coefficient (D) from the cyclic voltammograms of 3 mM Clarithromycin in the presence of 0.04 M B-R buffer (pH =2.5) with different scan rates at 30±1°C

S. No	Scan rate (mV/s)	pH = 2.5					
		First peak (Anodic)					
		E_{pa}^1 (mV)	I_{pa}^1 (µA)	$E_{p1/2}$ (mV)	E_{pa}- $E_{p1/2}$ (mV)	[a]α	[b]D×10^5 cm^2/s
1	20	1103±27	3.0±1.2	1030±15	94±16	1.0±0.5	1.5±0.3
2	100	1115±25	6±1.2	1253±24	138±13	0.7±0.8	2.0±1
3	200	1123±28	13±0.1	1282±18	159±16	0.6±0.2	3.4±2
4	300	1141±28	17±3	1310±27	169±15	0.6±0.1	3.6±1.1
5	400	1155±74	20±2	1334±24	179±16	0.5±0.1	3.7±1.2
6	500	1178±27	23±2	1350±12	172±11	0.6±0.2	4.0±1.0
		Second peak (Anodic)					
S. No	Scan rate (mV/s)	E_{pa}^2 (mV)	I_{pa}^2 (µA)	$E_{p1/2}$ (mV)	E_{pa}- $E_{p1/2}$ (mV)	[a]α	[b]D×10^5 cm^2/s
1	20	1251±17	7.0±0.1	1178±16	73±5	0.7±0.1	0.9±0.1
2	100	1387± 25	12±0.1	1314±17	73±4	0.7±0.8	6±2
3	200	1414±27	17±0.11	1340±16	74±6	0.6±0.2	10±2
4	300	1452±26	24±0.3	1375±19	77±9	0.6±0.1	10±4
5	400	1490±21	30±0.21	1412±17	78±8	0.6±0.1	10±2
6	500	1514±22	34±0.22	1428±15	86±9	0.6±0.2	11±3

Table 2. Values of heterogeneous rate constant (K^o) with 100mV/s at different pH

S. No	pH	First peak [1] (Anodic)	Second Peak [2] (Anodic)
		K^o×10^{-4} (cms^{-1})	K^o×10^{-4} (cms^{-1})
1	2.5	1.01	2.03
2	3.0	1.18	2.54
3	3.5	1.44	3.01
4	4.0	1.52	-
5	5.0	3.0	-

4. CONCLUSION

The exploration of electrochemical properties of the biologically active compounds has been carried out by cyclic voltammetery technique to investigate the 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 reactions.

According to the recent work Clarithromycin is represented irreversible oxidation process in B-R buffer. It was observed Clarithromycin during oxidation process two electrons were transferred while the electrochemical process is diffusion controlled. Effects of concentration, pH and scan rates on electrochemical process have also been observed.

These parameters explain 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 appropriate for quality control laboratories as well as pharmacokinetic studies. Moreover, this technique is proper alternative due to easy handling, time saving and cheaper as compare to other techniques such as HPLC or chromatography.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Florey K. Analytical profiles of drugs substance and excipients. 1996;24:47-49.
2. Avramov Ivic ML, Petrovic SD, Mijin DZ, Zivkovic PM, Kosovics IM, Drljevic KM, Jovanavic MB. Studies on electrochemical oxidation of azithromycin and Hemomycin at gold electrode in neutral electrolyte. Electrochim Acta. 2006;51:2407-2416.
3. Tripahi GK, Singh S. Formulation and in vitro evaluation of ph-sensitive oil-entrapped buoyant beads of clarithromycin. Tropical J. of Pharmacutical Research. 2010;9:533-539.
4. Hart JP. Electroanalysis of biologically important compounds. Ellis Horwood Pub., New York ed; 1990.
5. Kellner R, Mermet JM, Otto M, Valcarcel M, Widmer HM. Analytical chemistry: A modern approach to analytical science. 2nd Ed., Wiley-VCH Pub., Weinheim; 2004.
6. Wang J. Electroanalytical techniques in clinical chemistry and laboratory medicine. Wiley-VCH Pub, New York, Ed; 1988.
7. Ye BF, Zhang ZJ, Ju HX. Fluorescence study on the interaction between naproxen and yeast DNA. Chin Chin. J. Chem. 2005; 23:58.
8. Hope J, Eichhorn A. Comparative antimicrobial activity of the new macrolides against Borrelia burgdorferi. J. Microbiol. Infect. Dis. 1989;8:653.
9. Rastogi N, Goh KS. Effect of pH on radiometric MICs ofclarithromycin against 18 species of mycobacteria. Antimicrob. Agents Chemother. 1992;36:2841.
10. Rote AR, Pingle SP. Development and validation of bioanalytical method for determination of telmisartan and hydrochlorothiazide using HPTLC in human plasma. J. Cromatography. 2009; 877:3719-3723.
11. Ebraheem SAM, El- basher AA, Abdul- Enein HY. Spectrophotometric methods for the determination of gemifloxacin in pharmaceutical formulations. Acta. Pharm. Sinica part B. 2011;1:248.
12. The Indian Pharmaopeia commission, Central India Pharmacopeia Laboratory, Govt. of India Ministry of health & Family welfare, Ghaziabad, India Pharmacopeia, ed 7th,V-II. 2010;2010-1410.
13. Chio SJ, Kim SB, Lee HY, Na DH, Yoon YS, Lee SS, Kim JH, Lee KC, Lee HS. Column –Switching high – performance liquid chromatographic determination of clarithromycin in human plasma with electrochemical detection. Talanta. 2001; 54:377-382.
14. Dong SY, Xue CX, Huang TL. Electrochemical studies of the interaction of clarithromycin with bovine seum albumin. Anal. Sci., 2008;24:10871091.
15. SUN JJ, BAI Yu-w, LIU B, Bai B. Determination of clarithromycin by single – sweep oscillopolarography and its electrochemical behavior. Acta Chimica Sinica. 2004;1.
16. Avramovivic ML, Petrovic SD, Mijin DZ. A study of the electrochemical activity of some macrolide antibiotics on a gold electrode in a neutral electrolyte. J. Serb. Chem. Soc. 2007;72:1427-1436.

17. Hegde1 RN, Kumara BE Swamy2 Sherigara BS, Nandibewoor ST. Electro-oxidation of atenolol at a glassy carbon electrode. Int. J. Electrochem. Int. J. Electrochem. Sci. 2008;3:302-314.
18. Oliveira Brett AM, Diculescu VC, Piedade JAP. Electrochemical oxidation mechanism of guanine and adenine using a glassy carbon microelectrode. Bioelectro-chemistry. 2002;55:61.
19. Oliveira Brett AM, Piedade JAP, daSilva LA, Diculescu VC. Voltammetric determination of all DNA nucleotides. Anal. Biochem. 2004;332-321.
20. Oliveira Brett AM, Matysik FM. Sonoelectrochemical studies of guanine and guanosine. Bioelectrochem. Bioenergy. 1997;42:111.
21. Goyal RN, Kumar N, Singhal NK. Oxidation chemistry and biochemistry of indole and effect of its oxidation product in albino mice. Bioelctrochem. Bioenergy. 1998;45:47.
22. Nagaraj PS, Lokesh VS, Rajesh NH, sheranappa TN. Electrochemical oxidation of loop diuretic furosemide at gold electrode and its analytical applications. Int. J. Electrochem Sci. 2009;4:104-121.
23. Tesfaw B. Study of CE mechanism by cyclic voltammetry Cd(II)+ Aspartic acid system, Addis Ababa University School of Graduate Studies Department of Chemistry, Thesis; 2010.
24. Brett CMA, Brett AMO. Electrochemistry: Principles methods and applications. Oxford University Press; 1993.
25. Greef RP, Pletcher LM, Robinson J. Instrumental method in electrochemistry. Eillis Harwood, Chicherster; 1985.
26. Bard AJ, Faulkner LR. Electrochemical methods fundamentals and applications. John Wiley & Sons, New York, NY; 2001.
27. Azhar Ali S, Sami MA. Cyclic Voltammetric study of Bendrofluazide at a carbon past electrode. Pak. J. Pharm. Sci. 2000;13:21-37.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=1052&id=7&aid=9560