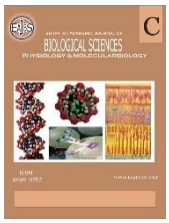
.

Citation: *Egypt.Acad.J.Biolog.Sci. (C.Physiology and Molecular biology) Vol. 15(1) pp509-521 (2023)*
DOI: 10.21608/EAJBSC.2023.303806

Egypt. Acad. J. Biolog. Sci., 15(1):509-521 **(2023)**

Egyptian Academic Journal of Biological Sciences
C. Physiology & Molecular Biology
ISSN 2090-0767
www.eajbsc.journals.ekb.eg



Determination of Azilsartan Medoxomil (anti-hypertension drug) by Cyclic Voltammetry Study and Biological Applications

Shihab A. Shihab* and Muthana S. Mashkour
Faculty of Science, Department of Chemistry, University of Kufa, Iraq
***E-mail:** shihabirsjwk1998@gmail.com

ARTICLE INFO
Article History
Received:25/4/2023
Accepted:6/6/2023
Available:11/6/2023

Keywords:
Electrochemistry, Cyclicvoltametery, Glassy carbon electrod(GCE), azilsartan medoxomil(AZL) and hypertension.

ABSTRACT

The purpose of this project is to examine the cyclic voltammetry (CV) analytical technique for the anti_thalassemia drug of azilsartan medoxomil by glassy carbon electrode (GCE) was described. The electrochemical performance of azilsartan medoxomil was studied by cyclic voltammetry technique. The ability of the electrode the determine azilsartan medoxomil under Optimized conditions in pH 12.699, scan rate 20mv/s, temperature 40 0C and interference have been studied. Where found the results that calibration curve of azilsartn medoxomil was linear in the concentrations 13.4×10-4-2.6×10-2 M, its detection limit was 8.46×10-11 M and LOQ was 2.82×10-10 M. The enthalpy ΔH was calculated to be (6.736 kJ. mol-1), and the entropy can be calculated to be (213.8 J. K-1 mol-1). The area of the electrode was calculated to be 0.0054 cm2 and the diffusion coefficient was 3.154×10-4 cm2sec-1. RSD% for bulk and form was less than 0.3%. The voltammogram for azilsartan medoxomil gives an irreversible process with a diffusion-controlled process. Finally, this technique has been applied to azilsartan medoxomil in pharmaceutical formulations.

INTRODUCTION

Hypertension is a progressive CV syndrome arising from complex and interrelated etiologies. Early markers of the syndrome are often present before BP elevation is sustained; therefore, hypertension cannot be classified solely by discrete BP thresholds. Progression is strongly associated with functional and structural cardiac and vascular abnormalities that damage the heart, kidneys, brain, vasculature, and other organs and lead to premature morbidity and death.7 Reduction of BP when target organ damage is demonstrable or the functional precursor of target organ damage is present and still reversible generally reduces the risk for CV events. Note that we separate elevated BP (one manifestation of the disease) from hypertension the disease. Hypertension is the most common modifiable risk factor for cardiovascular disease and death, and lowering blood pressure with antihypertensive drugs reduces target organ damage and prevents cardiovascular disease outcomes. Despite a plethora of available treatment options, a substantial portion of the hypertensive population has uncontrolled blood pressure. The unmet need of controlling blood pressure in this population may be addressed, in part, by developing new drugs and devices/procedures to treat hypertension and its comorbidities. In this Compendium Review, we discuss new drugs and interventional treatments that are undergoing preclinical or clinical testing for hypertension treatment.

New drug classes, eg, inhibitors of vasopeptidases, aldosterone synthase and soluble epoxide hydrolase, agonists of natriuretic peptide A and vasoactive intestinal peptide receptor 2, and a novel mineralocorticoid receptor antagonist are in phase II/III of development, while inhibitors of aminopeptidase A, dopamine β-hydroxylase, and the intestinal Na+/H+ exchanger 3, agonists of components of the angiotensin-converting enzyme 2/ angiotensin(1–7)/Mas receptor axis and vaccines directed toward angiotensin II and its type 1 receptor are in phase I or preclinical development. The two main interventional approaches, transcatheter renal denervation and baroreflex activation therapy are used in clinical practice for severe treatment-resistant hypertension in some countries. Renal denervation is also being evaluated for treatment of various comorbidities, eg, chronic heart failure, cardiac arrhythmias and chronic renal failure. Novel interventional approaches in early development include carotid body ablation and arteriovenous fistula placement. Importantly, none of these novel drug or device treatments has been shown to prevent cardiovascular disease outcomes or death in hypertensive patients.

Azilsartan medoxomil (AZL) is a chemically 2-ethoxy-3-[[4-[2-(5-oxo-2H - 1, 2, 4-oxadiazol-3-yl) phenyl]phenyl] methyl] benzimidazole-4-carboxylic acid. It was approved by the U.S. Food and Drug Administration(FDA) as Edarby tablets on 25 February 2011 to treat hypertension in adults. Azilsartan is an Angiotensin 2 Receptor Blocker. The mechanism of action of azilsartan is as an Angiotensin 2Type 1 Receptor Antagonist. The physiologic effect of azilsartan is by means of Decreased Blood Pressure. Theazilsartan is mainly used in the therapy of hypertension.

It is associated with a low rate of transient serum aminotransferase elevations but has yet to be linked to instances of acute liver injury and lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes.

Electrochemistry is a branch of chemistry that was founded in the late 19th and early 20th centuries to describe the relationship between electrical and chemical effects(Scholz 2015). Electrochemical techniques are strong and efficient analytical techniques that provide great sensitivity, accuracy, and precision with a wide linear dynamic range when using comparatively low-cost instrumentation(Farghaly, Abdel Hameed, and Abu-Nawwas 2014; Zadeh *et al.*,2022). A typical electrochemical detection system consists of three electrodes: a working electrode (WE), a reference electrode (RE), and a counter electrode (CE)(Bontidean *et al.* 1998; Huldani *et al.*,2022). working electrode because of its capability to stimulate electron transmission, and improve sensitivity and chemical inertness(Zare and Nasirizadeh 2010; Ansari *et al.*,2022). To enhance the detection limit, a glassy carbon electrode was developed in this study (Jain Rajeev and Rather 2011; Mohammed and Qasim, 2021). One of the types of voltammetry is Cyclic voltammetry(Kounaves 1997; Hafsan *et al.*,2022). Cyclic voltammetry is very suitable in determining the mode of transport for the system which is designed for two possible modes of transport, adsorption and diffusion (Nicholson 1965; Bokov *et al.*,2022).

UV spectroscopic method ,high-performance liquid chromatography HPLC (Sagiroglu, Onal, and Evrim Kepekci Tekkeli 2020), and spectrophotome ter with first-order derivative,1andHPTLC, RP-HPLC (Naaznee S Sridevi A2014) are some of the methods used to determine AZL in pharmaceutical formulations that have been published.

MATERIALS AND METHODS

Chemicals and Reagents:

Azilsartan medoxomil was provided by Interpharmachem of China. Where all of the solutions were made with deionized water. Drug-free serum forms were taken

from healthy volunteers and stored icy till the analysis. All solutions of this drug were prepared freshly at 0.05 M concentration, the stock solution was prepared at 0.027 M concentration by dissolved in 25 ml of Sodium hydroxide that was standardization by titrating it with HCl at a concentration of 0.1M to study the (effects of scan rate, pH, temperature, concentration, analytical application, and interferences). Finally, the samples were kept in a dark place at 4 0C till the study because the concentrations of azilsartin medoxomil solutions remained constant through time.

Apparatus:

Apparatus A DY2100 series potentiostate with glassy carbon (3mm) diameter electrode as working electrode, Ag/AgCl as reference electrode, and platinum electrode as auxiliary electrode was used to measure volumetrically. The primary transformation signal was Windows 10 (64-bit). A (Hanna- instrumental) was used as a digital pH meter a glass combination electrode served to carry out the pH measurements.

RESULTS AND DISCUSSION

The purpose of this study was to use cyclic voltammetry and calculate the active area of the electrode surface to determine AZL in pharmaceuticals (Exjade). In summary, we investigated the effects of scan rate, pH, temperature, concentration, and interferences.

Active Area of GCE Electrode:

The active area of the electrode was obtained by the cyclic voltammetric method using 5 mM K4Fe(CN)6 as a probe at different scan rates. For a reversible process, the following Randles–Sevcik formula can be used:

$Ipa = 0.4463(F\ 3/\ RT)^{1/2} n^{3/2} AD^{1/2} \upsilon^{1/2}$…….(3.1)

For 5 mM K4Fe(CN)6 in 0.1 M KCl electrolyte, T = 298 K, R = 8.314 J K^{-1} mol^{-1}, F = 96,485 C mol^{-1}, n = 1, D = 7.6 × 10^{-6} cm^2 s^{-1}, then from the slope of the plot of Ipa vs. $\upsilon^{1/2}$, relation, the electroactive area was calculated. In our experiment, the slope was 2 × 10^{-3} A $(V\ s^{-1})^{1/2}$ and the area of electrode was calculated to be(0.0054 cm^2).the lower the surface area value the electrode surface in Figure(1).

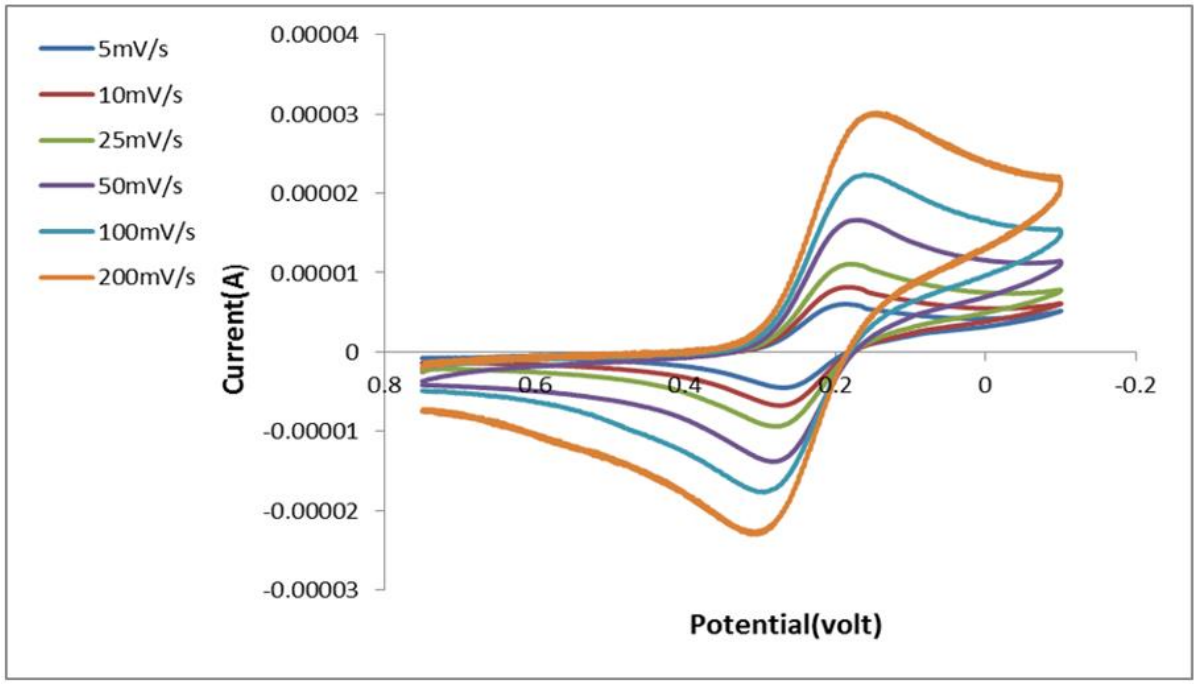


Fig.1 (A): Cyclic voltammograms of 5×10-3 mM K3 [Fe (CN) 6] at scan rates of (1)5, (2)10, (3)25, (4)50, (5) 100 (6)200 mV/s.

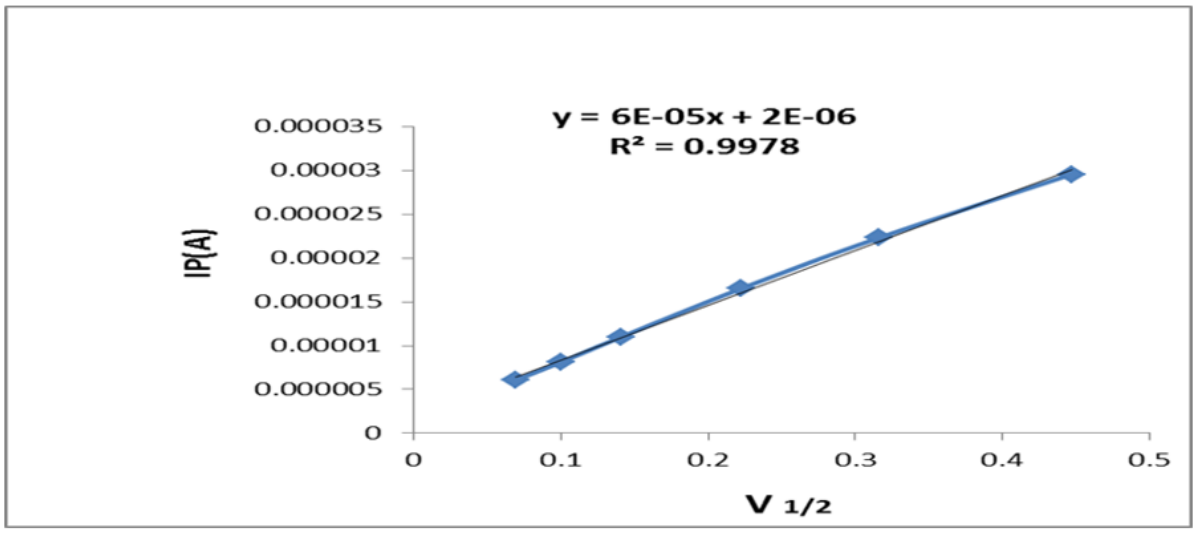


Fig.1 (B): Relationship between anodic peak current and square root of the scan rate.

Parameter Optimization for AZL:

Effect of Scan Rate:

Using the CV technique in 0.05M sodium hydroxide solution (pH 12.699), the effect of the potential scan rate on the GCE was investigated at various scan rates (5, 10, 20, 50, 100, 200, 500 and mV.s-1). The best scan rate according to Figure 2, was (100 mV.sec-1).

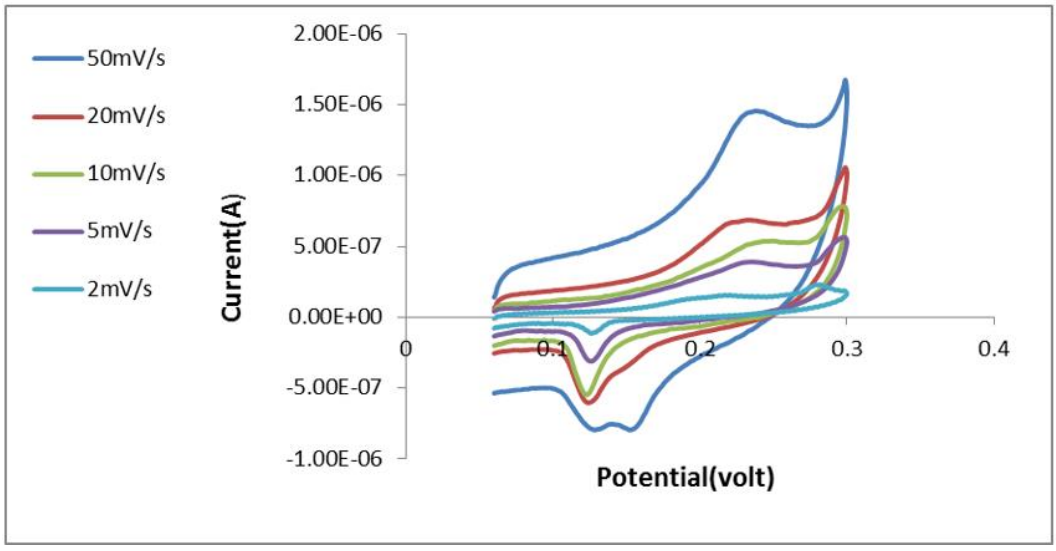


Fig. 2: Cyclic voltammogram showed the effect of scan rate at GCE electrode.

Figure 3 shows that the potential applied to Azilsartn medoxomil dissolved in 0.05 M NaOH solution increases as the scan rate increases, indicating that diffusion takes place on the electrode surface (Li *et al.*, 2019). The relationship shown in Figure 4 between the logarithm of current density for anodic peak and logarithm of scan rate, due to the Randles-Sevick equation in a linear diffusion controlled process (J α ν 1/2), for the adsorptive process (J α ν) (logJ α logν) (Morya *et al.* 2013). which conformed the following equation:

(R^2 = 0.9937) …. …. (2) Log J = 0.5727 log v + 1.2264

If the slope is near 0.5, the diffusion-controlled process is described, whereas the adsorption-controlled process is described by the slope is near 1.0 (Chrzescijanska *et al.* 2014). The slope in this study is 0.5727, indicating a diffusion-controlled process.

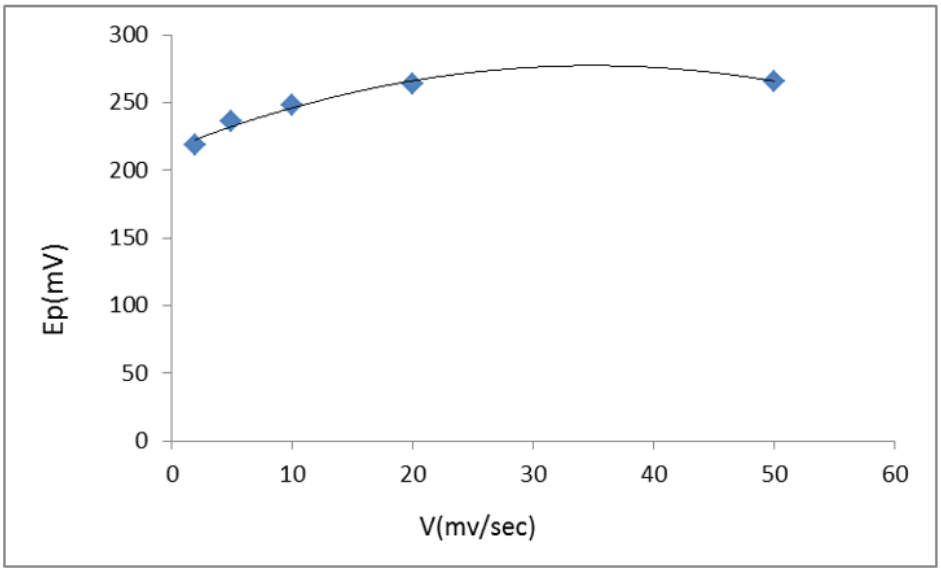


Fig.3: Relationship between (Ep) versus scan rate at GCE electrode.

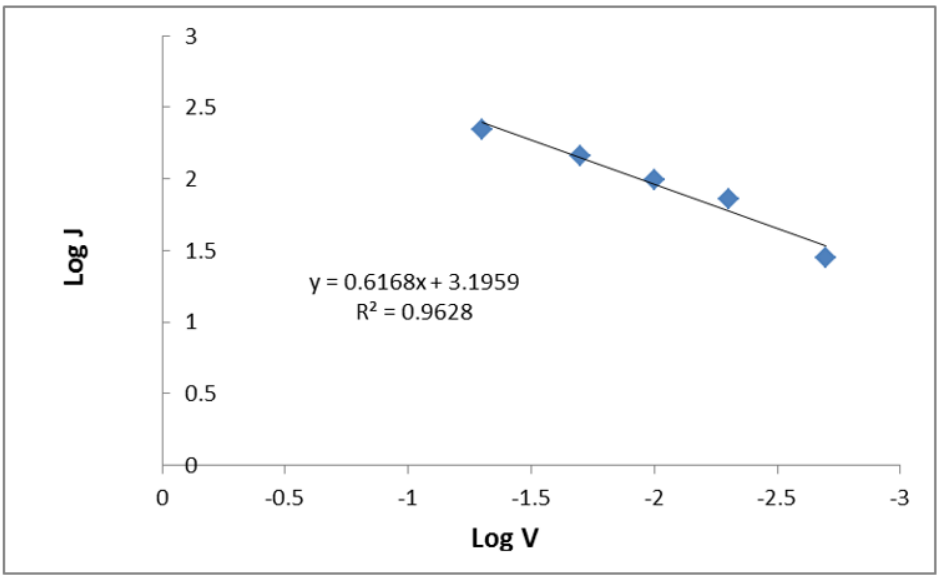


Fig.4: The effect of log current density vs log v at GCE electrode.

In the case of the irreversible process (Ep) peak potential is defined by Laviron (Shetti *et al.* 2019) and expressed in equation (3).

$Ep=E°+[2.303RT\alpha nF]\log[RTK0\alpha nF]+[RT\alpha nF]$ log v…… (3)

Where **E°** is the standard redox potential, **n** is the number of electrons transferred in the reaction, **k0** is the standard rate constant of the reaction, ***v*** is the scan rate, **α** the electron transfer coefficient, which can be calculated from the difference between the peak potential (Ep) and the half-wave potential (Ep/2) and the frequency can be calculated from the equation (4). The other symbols were used as R=8.314 JK-1mol-1, T=298 K°, and F= 96485C.mol-1. The value of E**0** can be determined from equation (3), The value of E**0** is 0.744v and the value of K**0** is 0.447 s-1. For irreversible electrode reaction, the value of α is (0.426) which is the number of electrons for oxidation peak 1.95 ≈ 2 have been observed which showed the transfer of two electrons in electro oxidation process of the AZL. The value of D0 was (3.154×10-4 cm2sec-1) in scan rate 20 mv/s.

$\alpha = 47.7\ Ep - Ep/2\ mV$ … … . (4)

Effect of pH:

The electrochemical study explained AZL in NaOH solution (0.1M) as a supporting electrolyte at various pH values (7-12.699), The measurement was made at 0.05 M using (GCE) electrode, pH 12.699 ~14 was obtained the maximum peak current for AZL at GCE in scan rate (20 mv/s) that shows in Figure 5 and change was detected in the oxidation peak currents with increasing pH values as ascertained in measurements with AZL. Furthermore, the *Ep* can be calculated from the following equation for a diffusion-controlled electrode(Ortaboy and Atun 2015) :

$$Ep = -0.05915\ P\alpha n\ pH \ldots\ldots. (5)$$

The p value at the GCE electrode can be calculated at 0.556 using equation (6) or the relationship between Ep and pH. Because the p value is less than 1, this value indicates no protonation process. At pH levels below 7, the azilsartan medoxomil solution became turbid, probably because of the low solubility of azisartan medoxomil at these pH values. At pH levels above 10, the currents of oxidation peaks of azilsartinmedoxomil were increased. Thus at pH =11 the value of the potential increases with pH as we notice in the Figure 6.

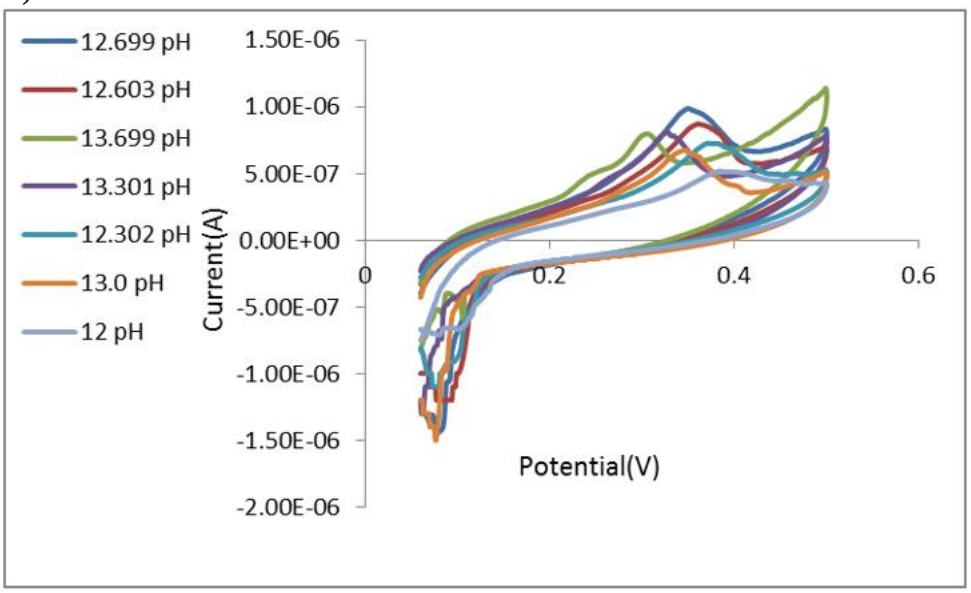


Fig.5: The effect of pH at GCE electrode for scan rate20mv/.

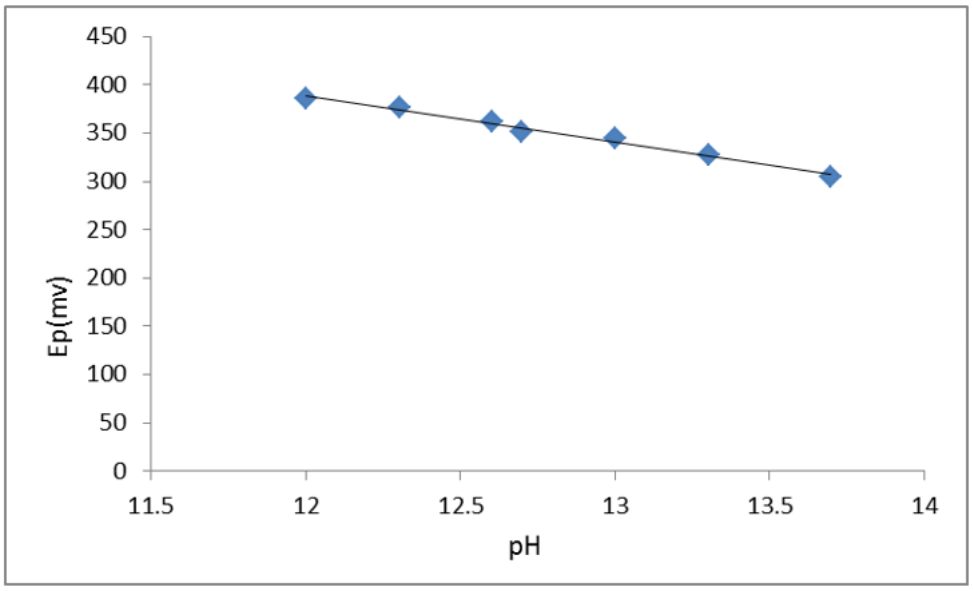


Fig.6: Effect of pH in the peak potential at GCE in *2*0mv/s.

So the suggestion of the electro-oxidation mechanism of reaction can be illiterate in Figure 7 .The results can be attributed to the presence of two phenolic groups in the deferasirox structure, which create radical cations during the electro-oxidation process. The carbon is then powerfully and irreversibly adsorbed by these radical cations (Longo-Mbenza *et al.* 2004).

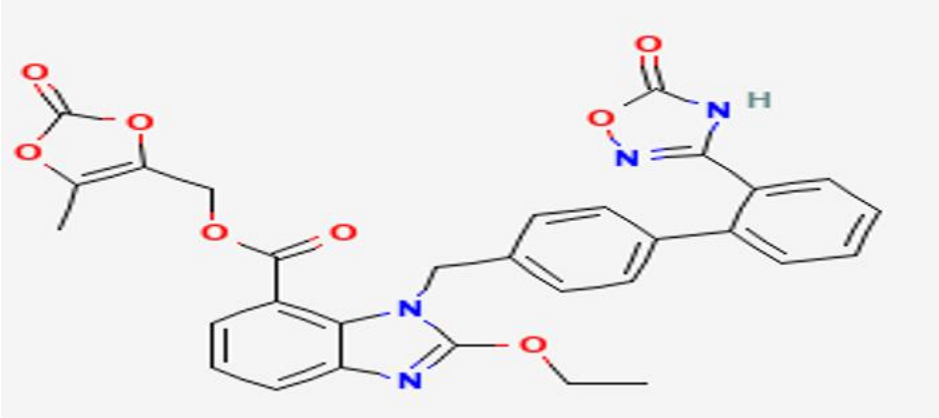


Fig.7: The suggestion of the electro-oxidation mechanism of reaction.

Effect of Temperature:

The electrochemical behavior of azilsartan medoxomil on the GCE electrode at varying temperatures (10, 20, 30,35, 40) 0C was shown in Figure 8. We noticed a gradual increase in the current with temperature when the temperature reached 30 0C maximum this indicates that the best temperature was 40 0C for GCE electrode.

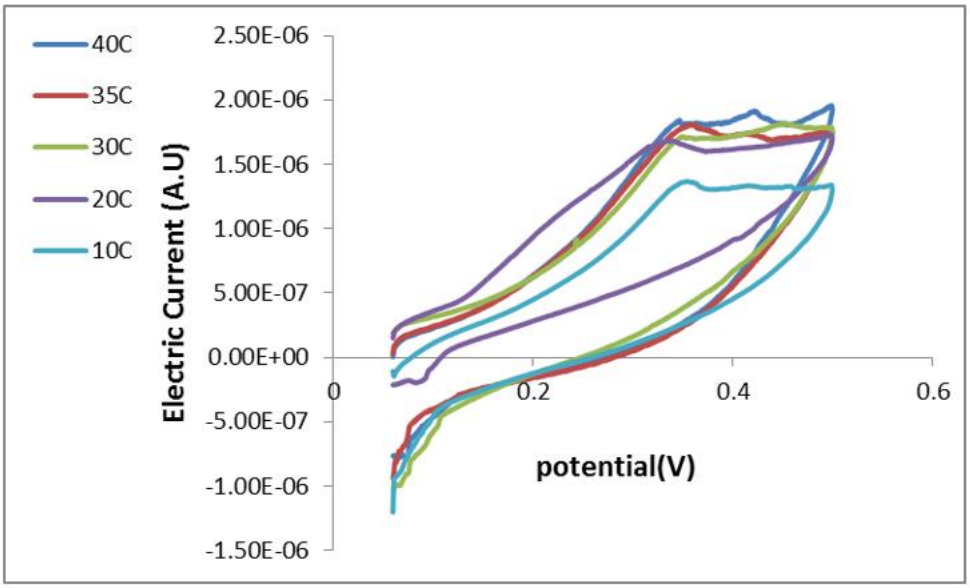


Fig.8: The effect of temperature at GCE electrode for scan rate 20mv/s.

The activation energy was calculated to be (535.5 kJ. mole-1) for GCE electrode. The activation energy obtained is large, which indicates that the electrochemical reaction is more temperature-dependent.

From the slope in Figure 9, the enthalpy ΔH of the electrochemical reaction of azlsartan medoxomal is calculated to be

(6.736 kJ. mol-1), and from the intercept, the entropy can be calculated to be (213.8 J. K-1 mol-1). The positive value of ΔH refers to endothermic reaction and the positive value of ΔS refers to that the disorder is increasing from reactants to products(Molina *et al.* 2020). So the change in Gibbs free energy can be simply calculated from equation (6) to be (-58.04 kJ.mol-1) for GCE electrode.

$\Delta G=\Delta H-T\Delta S$……. (6)

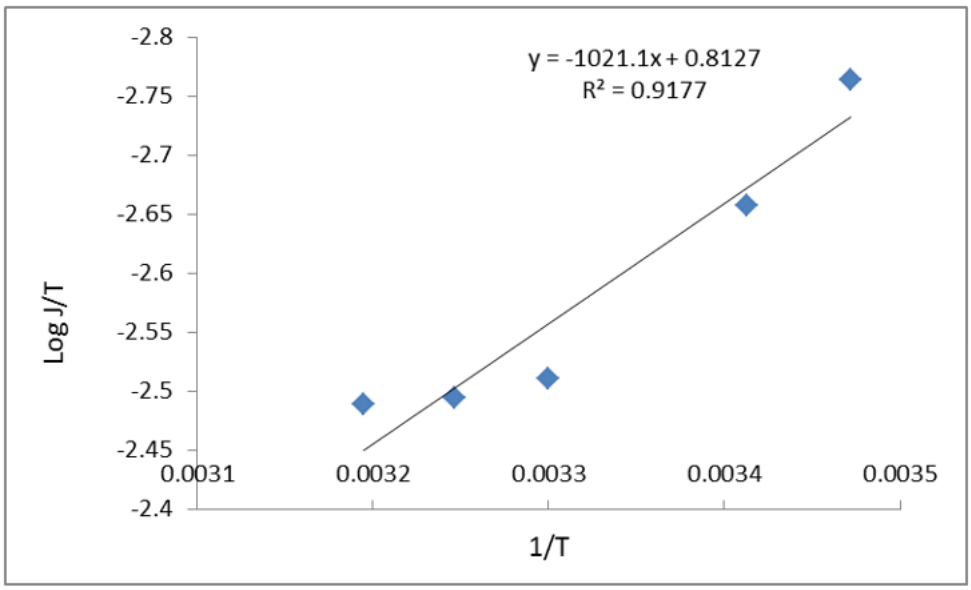


Fig.9: Relationship between log J/T, and 1/T at GCE for scan rate 20mv/s

Calibration Curve:

The effect of the concentration of deferasirox versus current density on the GCE-MWCNTs electrode was investigated using CV method under the optimum condition (pH 12.699 ~13), (*v* 20 mV.sec-1), (T 40 °C), the calibration plot was describing by the following equation:

J(μA) = 0.1273 Conc. + 98.685 R^2 = 0.9854 ……..… (7)

A linear calibration plot was obtained for AZL(Fig.10), the properties of the plot graph for AZL in Figure.11 is in the range (13.4×10-4-2.6×10-2 M). The LOD is calculated to be (8.46×10-11 M) from 3σ /m, and also LOQ is calculated to be (2.82×10-10 M) from 10σ /m where **m** is the slop. The characteristics of AZL are listed in Table (1).

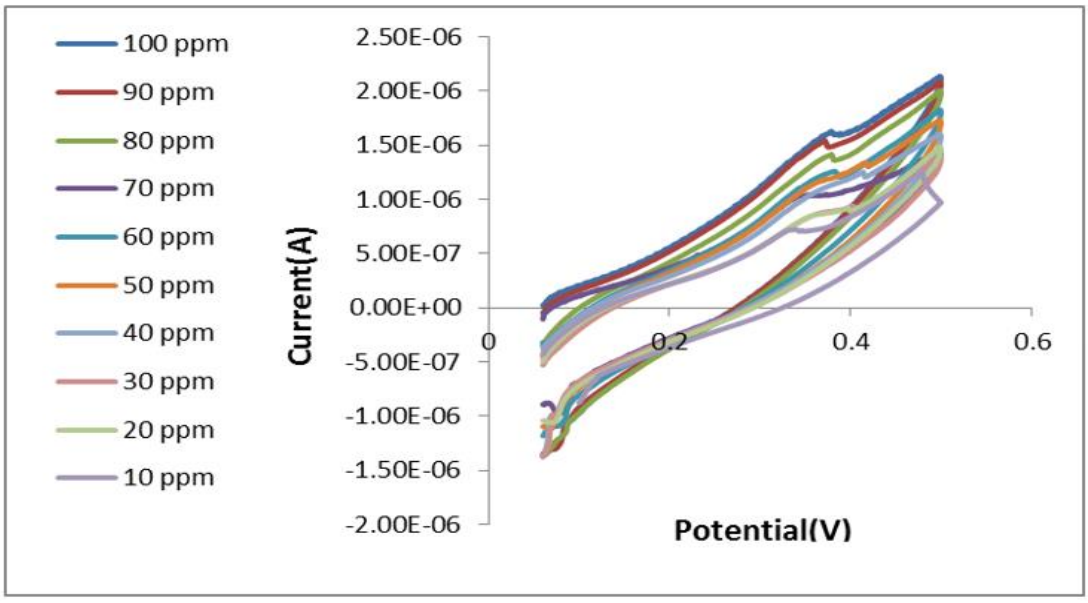


Fig.10 :Calibration curve 50 ppm obtained AZL

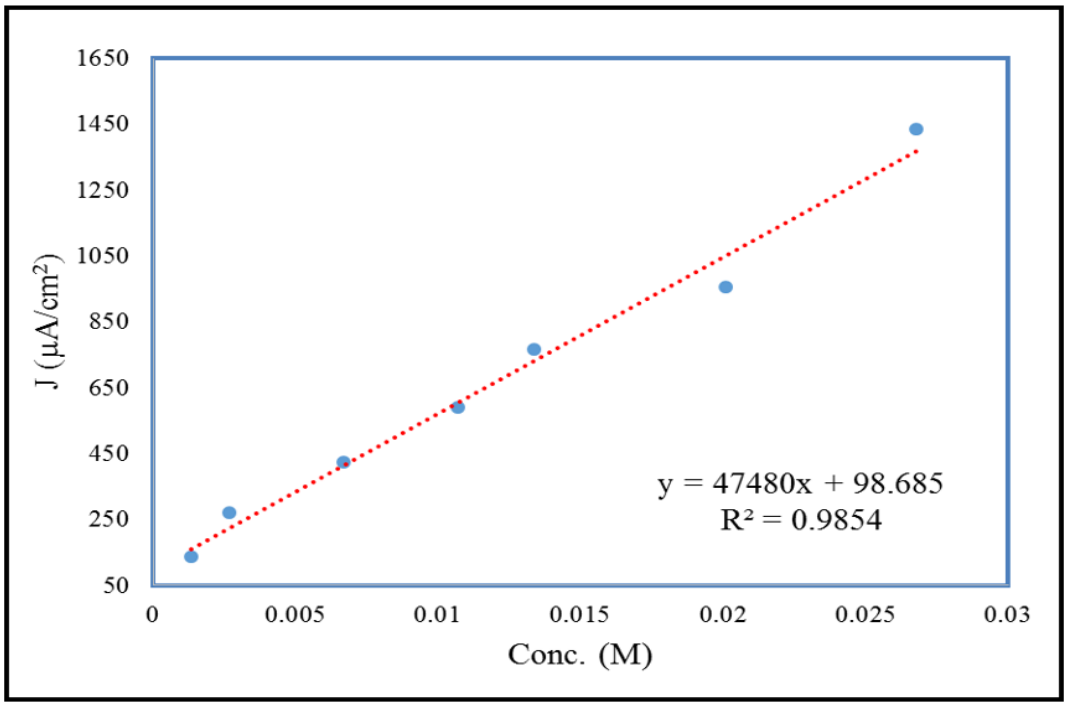


Fig.11: Relationship between J, and conc. at GCE for scan rate 20mv/s

Table 1: Analytical parameters of the calibration plot.

GCE	parameter
13.4×10-4-2.6×10-2	Linearity range (M)
47480	Slope
98.685	Intercept (µA)
0.9854	Correlation coefficient (R2)
8.46×10-11	LOD (M)
2.82×10-10	LOQ (M)
1.349×10-6	SD (M)
3.372×10-9	RSD%

Accuracy and Precision In Analytical Applications:

In order to assess the method's precision and accuracy, five duplicate measurements for the added weights 40-80 mg in analytical applications, were analyzed at GCE. The method validity was applied by taking two types are Exjade and Ipijade which available from local pharmacies were analyzed AZL content for their labeled content. The recoveries and relative standard deviation are labeled and according to the following values in Table 2. This indicates good accuracy and precision for the suggestion method.

Table 2: The analytical characteristics of AZL

Serum	Urine	Form	Bulk	
25 50 100	25 50 100	80 40	80 40	Added (mg)
24.0 49.5 100.5	25.9 50.5 98.5	80.8 39.9	79.8 40.1	Found (mg)
3	3	2	2	N
96.000 99.000 100.500	103.600 101.000 98.500	98.000 98.400	99.840 100.040	Average recovery %
98.500 2.2912 2.3260	101.033 2.5501 2.5240	98.200 0.2828 0.2879	99.940 0.1414 0.1410	Mean S.D RSD %

Interferences:

The interference of many possible potentially co-interfering compounds on the oxidation of AZL was performed. Interferences oxidation response does not interfere with AZL oxidation signal. Figure 12 show the interferences study of AZL at 1.34×10-3 M concentration, which was established by adding several potentially co-interfering compound into 0.05M of NaOH solution. The formulation of the pharmaceutical (Mannitol, fumaric acid, MCC, HPC, Microcrystalline cellulose, NaOH, Magnesium stearate, and Lactose). These compound solutions were produced fresh at pH 12.699 and 25 0C in 25 mL of (0.05M) sodium hydroxide solution scan rate of 20 mV.sec-1.

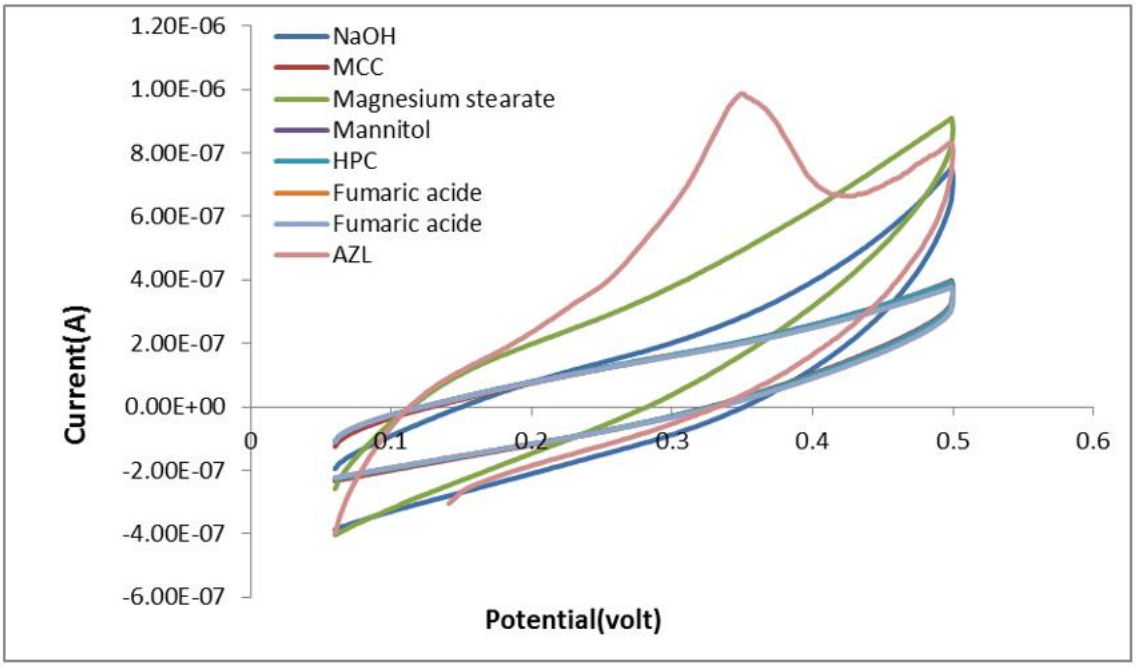


Fig..12: The effect of interferences on AZL in 500ppm.

Conclusions

The electrochemical study of Azilsartin medoxomil at GCE electrode was described and discussed by cyclic voltammetry, based on the diffusion behavior of azilsartin medoxomil onto the GCE surface. This technique a fully validated, simple, sensitive, selective, fast and low-cost for the determination of azilsartin medoxomil in bulk form, urine and serum.

REFERENCES

Ali.R, and Phase. I. 2006. The American, Advanced Rcc. "1 1.1 Scientific Discussion." : 1–49.

Ansari. M, Taban, T..Z. et al. (2022). Anticancer Drug-Loading Capacity of Green Synthesized Porous Magnetic Iron Nanocarrier and Cytotoxic Effects Against Human Cancer Cell Line. *Journal Cluster Science,* 34(1). DOI: 10.1007/s10876-022-02235-4

Availability Ali.M, 2011; 76 FR 14024:1–12Food and Drug Administration and the Department of Health and Human Services. Notice. *Guidance for Industry on Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims*; ; 76 FR 14024:1–12.

Chou.T. C, and Paul .T. 1984. "Quantitative Analysis of Dose-Effect Relationships: The Combined Effects of Multiple Drugs or Enzyme Inhibitors." *Advances in Enzyme Regulation*, 22(C): 27–55.

Chrzescijanska E. , Elzbieta. K. and Jacek. R. 2014. "Study of Acetylsalicylic Acid Electroreduction Behavior at Platinum Electrode." *Journal of Electroanalytical Chemistry*,713:17–21.

Dmitry O. Bokov,.A. , Jalil, F. ,Mustafa Z, Wanich. S, Supat C., Maytham T , Parvaneh .D (2022) Ir-decorated gallium nitride nanotubes as a chemical sensor for recognition of mesalamine drug: a DFT study, *Molecular Simulation,* https://doi . org/10.1080/08927022.2021.2025234

Farghaly. O. A., Abdel. H and Abd A. H. 2014. "Analytical Application Using Modern Electrochemical Techniques." *International Journal of Electrochemical Science,* 9(6): 3287–3318.

Hafsan. H, Dmitry .W ,Mustafa. M, Suksata.H, Majdi.G, Abdulad.T,

Jalil,M. T ,Mahboubeh. B (2022). Dietary Dracocephalum kotschyi essential oil improved growth, haematology, immunity and resistance to Aeromonas hydrophila in rainbow trout (Oncorhynchus mykiss). *Aquaculture Research,* 53:3164–3175. DOI: 10.1111/are. 15829

Hajjizadeh, M. . 2008. "Electrocatalytic Oxidation and Determination of AZL and Deferiprone on a Nickel Oxyhydroxide-Modified Electrode." *Analytical Biochemistry,* 373(2): 337–48.

Huldani. H , Bokov.D, Abdelbasset. W, Shalaby. M, Thangavelu. L, Qasim.. M (2022). Application of extracellular vesicles derived from mesenchymal stem cells as potential therapeutic tools in autoimmune and rheumatic diseases. *International Immunopharmacology,* 106, 108634.

Jain R, and Jahangir A. R. 2011. "Voltammetric Determination of Antibacterial Drug Gemifloxacin in Solubilized Systems at Multi-Walled Carbon Nanotubes Modified Glassy Carbon Electrode." *Colloids and Surfaces B: Biointerfaces,* 83(2): 340–46.

Jain, R, and Sanjay. S. 2012. "Glassy Carbon Electrode Modified with Multi-Walled Carbon Nanotubes Sensor for the Quantification of Antihistamine Drug Pheniramine in Solubilized Systems." *Journal of Pharmaceutical Analysis,* 2(1): 56–61. http:// doi.org/10.1016/j.jpha. 2011.09.013.

Kannel W.B.1996 Blood pressure as a cardiovascular risk factor: prevention and treatment. JAMA.; 275: 1571–1576.

Kounaves, S. P. 1997. "Voltammetric Techniques." Handbook of instrumental techniques for analytical chemistry, 10(30): 709–26.

Li. K.. 2019. "Evolution of the Electrochemical Interface in Sodium Ion Batteries with Ether Electrolytes." *Nature Communications,* 10(1). .

Longo.M, Bgyvf. E. 2004. "Gallbladder Disease in Young Congolese with Sickle Cell Anemia: An Ultrasound Survey." *Journal of Tropical Pediatrics,* 50(2): 73–77.

Moffat. A, David. O and Brian. W. 2011. "Clark's Analysis of Drugs & Poisons." : 243–57.

Molina.V. 2020. "Deficits of Entropy Modulation of the EEG: A Biomarker for Altered Function in Schizophrenia and Bipolar Disorder?" *Journal of Psychiatry and Neuroscience,* 45(5): 322–33.

Morya, G. L. 2013. "Electrochemical Behavior and Validated Determination of the Azathioprine in Bulk Form and Body Fluids." *Der Pharmacia Sinica,* 4(3): 80–94.

Nicholson.P, Richard S. 1965. "Theory and Application of Cyclic Voltammetry for Measurement of Electrode Reaction Kinetics." *Analytical Chemistry,*37(11):1351–55.

Ortaboy, S, and Gülten. A. 2015. "The Electrochemical Behavior of Co(TPTZ)2 Complex on Different Carbon Based Electrodes Modified with TiO2 Nanoparticles." *Materials Chemistry and Physics,* 156: 129–40. .

Parvizi. F. G, and Reza. E S. 2018. "Multiwall Carbon Nanotube Paste Electrode as a Sensor for Sensitive Determination of Deferasirox in the Presence of Uric Acid: Application for the Analysis of Pharmaceutical and Biological Samples." *Turkish Journal of Chemistry,* 42(2): 493–504.

Rezaei. B., and Damiri.S. 2008. "Voltammetric Behavior of Multi-Walled Carbon Nanotubes Modified Electrode- Hexacyanoferrate(II) Electrocatalyst System as a Sensor

for Determination of Captopril." *Sensors and Actuators, B: Chemical*, 134(1): 324–31.

Sa.G, Ali. A, Cem. O, and Evrim. K. T. 2020. "Liquid Chromatographic Analysis for the Determination of AZL in Pharmaceutical Formulations and Spiked Plasma Samples Using Dansyl Chloride Reagent." *Journal of Chemical Metrology*, 14(1): 35–41.

Scholz, F. 2015. "Voltammetric Techniques of Analysis: The Essentials." *ChemTexts*, 1(4): 1–24.

Shetti N. P. 2019. "Electrochemical Detection and Degradation of

Textile. D ,Congo .R(2018) at Graphene Oxide Modified Electrode." *Microchemical Journal*,146:387–92. Societ

Zadeh, F. , Bokov.D, Salahdin,.O, Abdelbasset. W, Jawad. M, Kadhim, M, Khatami.M (2022). Cytotoxicity evaluation of environmentally friendly synthesis Copper/Zinc bimetallic nanoparticles on MCF-7 cancer cells. *Rendiconti Lincei Scienze Fisiche e Naturali*, 1-7.

Zainab .I and Maytham. T (2021) Hormonal profile of men during infertility. *Biochemical. CellularArchives*,21, 2895-2898.

Zare. H, and Navid. N. 2010. "Simultaneous Determination of Ascorbic Acid, Adrenaline and Uric Acid at a Hematoxylin Multi-Wall Carbon Nanotube Modified Glassy Carbon Electrode." *Sensors and Actuators, B: Chemical*, 143(2): 666–72.