Journal of Pharmaceutical, Chemical and Biological Sciences
ISSN: 2348-7658
Impact Factor (GIF): 0.615
Impact Factor (SJIF): 2.092
June-August 2015; 3(2):221-229
Available online at http://www.jpcbs.info

Original Research Article

Interaction of Anticancer Drug Letrozole with Ds-DNA Analyzed by Electrochemical Methods

Y. Brightson Arul Jacob[1*], J. Jeyasundari[2]

[1]Department of Chemistry, The American College, Madurai-625002, Tamilnadu, India
[2]Department of Chemistry, NMSSVN College, Madurai-625019, Tamilnadu, India

***Corresponding Author:** Y. Brightson Arul Jacob, Department of Chemistry, The American College, Madurai-625002, Tamilnadu, India

Received: 13 June 2015 Revised: 11 July 2015 Accepted: 18 July 2015

ABSTRACT

Letrozole is cheaper alternatives to anthracycline drugs. These drugs closely resemble anthracycline drugs both from a structural and functional point of view. Electrochemical behaviour of anticancer drug was studied at physiological pH using cyclic voltammetry. An electrochemical study on the interaction of the Letrozole with calf thymus DNA was carried out. The binding of Letrozole with calf thymus DNA was studied and compared with the binding ability. A cyclic voltammetric study provides a very low LOD and LOQ values for the determination of Letrozole.

Keyword: Letrozole; calf thymus ds-DNA; Phosphate buffer solution; cyclic voltammetry

INTRODUCTION

In the last decades, much attention was paid to the binding of small molecules with DNA, as a result of obtained advantages of these molecules as potential drugs. Since the concept of intercalation into DNA was first formulated by Lerman in 1961 [1]. It has become widely recognized that many compounds of pharmacological interest, including anticancer drugs and antibiotics correlate their biological and therapeutic activities with the ability of intercalative interaction with DNA [2]. This non covalent binding has an important function in life phenomena at the molecular level, deciding the interaction specificity of drug with DNA.

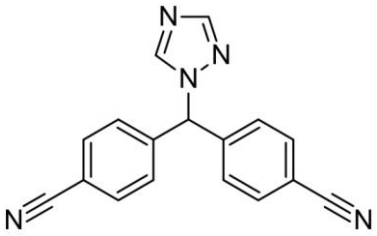
Anthracycline drugs, the most widely used anticancer agents [3, 4], get limited in their use due to high cost and cardiotoxic properties [5, 6]. Although the exact mechanism by which anthracyclines exert their anticancer activity is still uncertain [7], dominant amongst various

mechanisms appear to involve impairment of topoisomerase-IIα activity [8, 9], that is consistent with observed DNA intercalation and nuclear localization of the drug [10–12]. Biochemical studies show that the drugs inhibit both DNA-directed DNA synthesis [13] and DNA-directed RNA synthesis [14], presumably by their ability to interact with the DNA template primer [15, 16]. Owing to aforesaid reasons, research on the interaction of anthracyclines and their analogues with DNA is being actively pursued [16].Chemotherapeutic efficiency as well as cardio toxicity of anthracycline drugs is associated with electron transfer processes, which shows a very good correlation with the redox behavior of the molecules [17–20]. Owing to one electron reduction, the quinone moiety in these drugs is converted to semi quinone playing a major role in determining chemotherapeutic efficiency and toxicity in cellular systems [21, 22]. Analogues of anthracyclines, the hydroxy-9, 10-anthraquinones and their complexes, were reported to be suitable radio sensitizers [23–25], a phenomenon, also linked to electron transfer processes. In order to develop cost effective and also efficient substitutes of anthracycline drugs, different analogues are being tried clinically [4, 26].The aim of our study was to calculate the binding constant of anticancer drug of letrozole shown in scheme 1 and 2 with ds-DNA

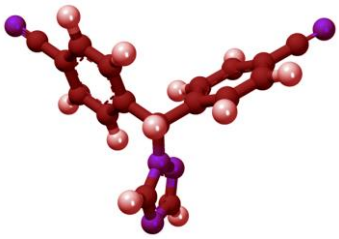
MATERIALS AND METHODS

Preparation of drug & buffer solution

The drug Letrozole has been purchased from the local pharmaceuticals and was used for the study. The structure of Letrozole and the ball stick model is shown in the scheme 1 and 2. The standard solution of 0.1M Letrozole was prepared by dissolving Letrozole in double distilled water and then it was stored in a refrigerator. All reagents were of analytical grade and used without further purification. Phosphate buffer was prepared using deionized water.



Scheme 1: Structure of letrozole



Scheme 2: Ball-and-stick model of the Letrozole molecule

Phosphate buffer was prepared using equimolar mixture of 0.1M potassium dihydrogen orthophosphate and 0.1M dipotassium hydrogen phosphate. By varying the concentration of the two components this buffer was prepared for pH varying from 5-8.

Preparation of calf thymus double stranded DNA (ct-ds-DNA)

The ct-ds-DNA was purchased from Biotech solutions, Bangalore, India and used for the study. 10µl of ds-DNA was taken from the stock solutions and made upto 10ml in a standard flask and was used for the study. The concentration of ct-DNA was measured by using its known extinction co-efficient at 260nm (6600 $m^{-1}cm^{-1}$). The absorbance at 260nm for ds-DNA was measured to check its purity [27-29].

Kinetics and electrochemical behavior of letrozole

For voltammetric measurements, the test solution was placed in a voltammetric cell of volume 13ml and deoxygenated by bubbling nitrogen for 10 min. During measurements, a

stream of nitrogen was passed over the solution. All experiments were carried out at room temperature. Cyclic voltammetric behaviour of 0.1M Letrozole was studied by varying the buffers, pH, scan rate and concentration. Bare glassy carbon electrode (GCE) was used as the working electrode for this study [30].

Effect of buffers and pH

Phosphate buffer have been chosen for this study. The pH was also varied using the phosphate buffer and best signal was noticed at pH 7.1. Letrozole was electroactive only in phosphate buffer at pH 7.1, therefore this buffer was chosen for further study [31].

Effect of concentration

In order to study the limit of detection (LOD) and limit of quantification (LOQ) the study on the effect of concentration was carried out [32]. Linear regression analysis of the data gave the following equation [33, 34];

i_p (µA)= 0.0626 C(M)+ 0.8905 ,(R^2 = 0.9128)

The sensitivity of the method was evaluated by determining the limit of detection (LOD) and limit of quantification (LOQ),LOD =3xSD/b; LOQ=10xSD/b [32].In order to study the interaction of Letrozole with ds-DNA, 1ml of $8.1818x10^{-6}$M solution of DNA was added with 1.5ml of 0.1M Letrozole in 5ml of phosphate buffer at pH 7.1.

RESULTS AND DISCUSSION

Influence of buffer

The cyclic voltammogram of Letrozole on a bare GCE in phosphate buffer (pH 7.1) is shown in figure1. It is clear that the electrochemistry of Letrozole on the bare GCE shows an oxidation peak at E_{pa}= 0.3754V and it is due to the oxidation of Letrozole. The number of electron transferred (n) and α transfer coefficient were calculated as 1 and 0.6271.

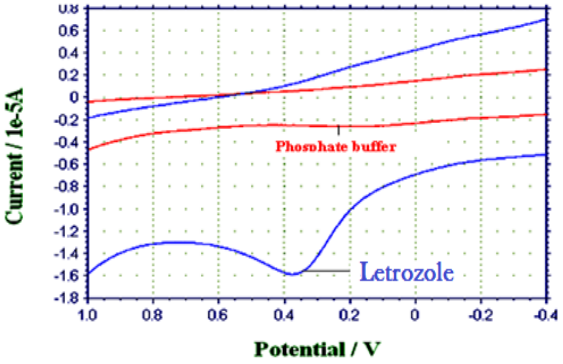


Fig1: Cyclic voltammogram of 0.1M Letrozole in Phosphate buffer at pH 7.1

Influence of scan rate

The scan rate is probably the most important experimental parameter for evaluating the effects due to adsorbed reactant and/or due to reaction at the electrode via diffusion. Figure 2 shows that the peak currents for the oxidation of Letrozole increases with increasing the scan rate from 25 mVs^{-1} to 500 mVs^{-1} [36, 37].

Figure3 represents the plot of the irreversible oxidation [38] currents (i_p) verses scan rate (v) yield straight line in the range from 25 to 500 mVs^{-1} and the corresponding regression equation is,

i_{pa} (µA)=0.045v (mV), R^2 = 0.875

Furthermore, it was observed that the oxidation peak current of Letrozole (i_p) varies linearly with $v^{½}$ (R^2=0.905) rather than v (R^2=0.875).This result indicated that the electrode process was controlled by diffusion process [39]. The following formula has been used to calculate the surface concentration of the drug,

$i_p = n^2F^2A\Gamma v/4RT$

According to the data obtained in cyclic voltammetry experiments, using the above formula the value of Γ was calculated as $3.8034x10^{-7}$ $mol^{-1}cm^{-2}$.

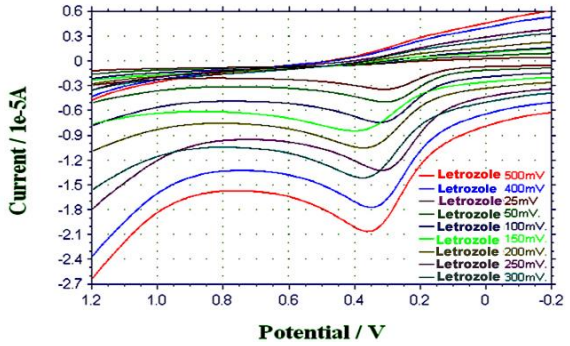


Fig. 2: Cyclic voltammogram of 0.1M Letrozole

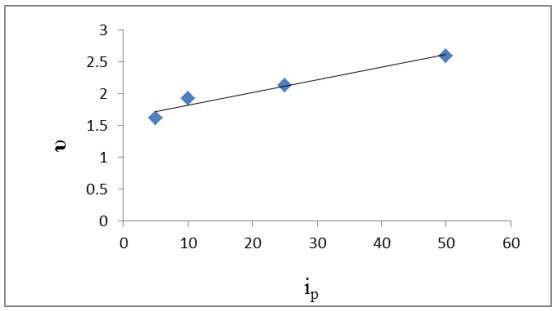


Fig 3: Plot of i_p Vs υ for 0.1M Letrozole at different Scan rates

The diffusive nature of the drug at the electrode surface was again confirmed from the slope value of the plot of logarithm of peak current (log i_p) vs logarithm of scan rate (log v). The plot of logarithm of peak current (log i_p) versus logarithm of scan rate (log v) gave a slope of 0.6003 (figure 4), which is close to the theoretical value of 0.5. That is expressed for an ideal reaction for the diffusion controlled electrode process [40]. The equation obtained is,

log i_{pa}(μA) = 0.600 log v (mVs^{-1}) - 0.332 , R^2 = 0.991

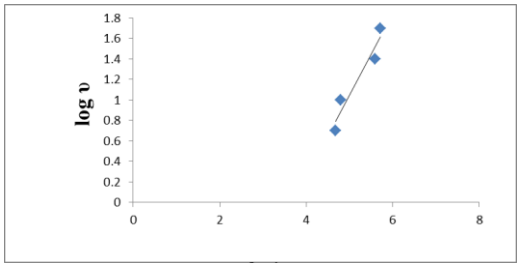


Fig 4: Plot of log i_p Vs log υ for 0.01M Letrozole

The diffusion coefficient of the drug was determined by using the reduced form of Randles-Sevcik equation (Potential Sweep Techniques), $i_p = 2.69x10^5\ n^{3/2}\ A\ D_0^{1/2}\ v^{1/2}C_0$. Where i_p, the peak current density is in Acm^{-2}, D is in cm^2S^{-1}, v is in VS^{-1} and C_o is in mol cm^{-1} [41]. From the slope (1.284) value of the plot (figure 5) of i_p versus $v^{½}$, the D_0value was calculated and is ($2.6894x10^{-6}$ cm^2 s^{-1}), the cyclic voltammetric experiments showed that both peak potential (E_{pa}) and peak current (i_{pa}) of Letrozole was in relation to the scan rate (v). The relationship between E_{pa} and log $v^{½}$, over the range 25mV to 500mV was discussed as follows. For an irreversible anodic reaction, the following equation may be used to calculate the rate constant for the heterogeneous electron transfer process [42],

$E_{pa} = E^0 + RT/[(1-\alpha)nF]\{0.780 + \ln(D1/2/k^0) + \ln[(1-\alpha)nFv/(RT)]^{1/2}\}$

α is the transfer coefficient, n is the number of electrons transferred per mole before the rate determining step, According to the above equation, the curve of E_{pa} Vs log $v^{½}$ shown in figure 6 should be linear and the k^0, the heterogeneous rate constant was calculated from the intercept and is $1.2320x10^{-2}cms^{-1}$

The calculated values of LOD and LOQ are $4.4406x10^{-8}$M and $14.802x10^{-8}$M respectively. The very low values of LOD and LOQ show the high sensitivity of the proposed method for the determination of Letrozole

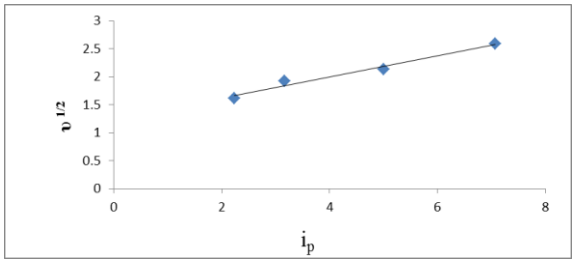


Fig 5: Plot of i_p log $υ^{½}$

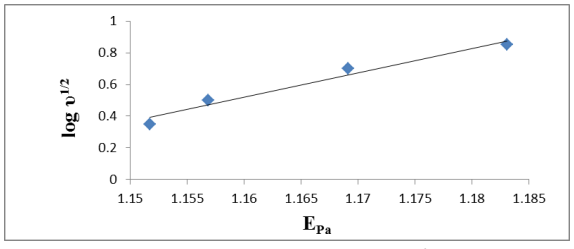


Fig 6: Plot of E_{pa} log $υ^{½}$

Kinetics of the interaction of letrozole with ds-DNA

The voltammetric behavior of the Letrozole and Letrozole DNA complex has been depicted in table 1. The decrease in peak current of Letrozole upon addition of ds-DNA into the Letrozole solution is maximum at pH 7.1. Under these conditions, the dramatic changes of cyclic voltammetric behavior of Letrozole in the presence of ds-DNA were occurred. Figure 7 shows the cyclic voltammetric behavior of Letrozole while increasing concentration of ds-DNA from 1.0909 x10^{-6}M to 3.5573 x10^{-6}M

Table 1: Voltammetric behaviour of Letrozole and Letrozole -DNA Complex

Scan rate v (V s-1)	Letrozole		Letrozole DNA Complex	
	E pa (V)	i pa (µA)	E pa (V)	i pa (µA)
0.025	0.3104	3.357	0.3068	3.456
0.050	0.3091	4.943	0.2664	4.012
0.100	0.3291	7.398	0.3209	5.502
0.150	0.4029	8.457	0.3370	6.966
0.200	0.3734	10.53	0.3470	8.283
0.250	0.3289	13.14	0.3581	9.527
0.300	0.3734	14.05	0.3601	10.32
0.400	0.3415	17.64	0.3195	13.83
0.500	0.3619	20.61	0.2193	18.00

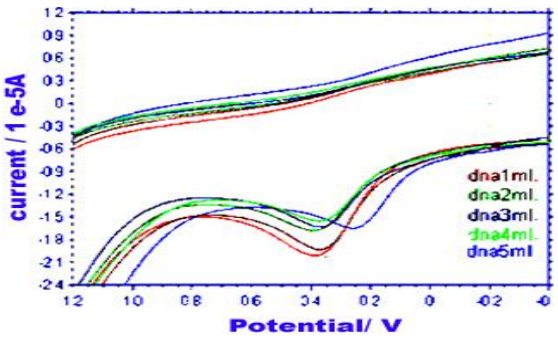


Fig 7: Cyclic voltammogram of 0.1M Letrozole in the presence of increasing concentration of ds-DNA

When ds-DNA is added to the solution of Letrozole, the peak current height decreases and shifts of peak potentials from 0.3664V to 0.2571V was noticed. At 3.5573 x10^{-6}M concentration of ds-DNA maximum shift in peak potential to the negative potential side was noticed. This shows the binding was maximum at this concentration. The anodic peak current decreasedto -1.614 x10^{-5} A in the presence of ds-DNA. According to these observations, it seems that the decrease of peak current of Letrozole after an addition of excess of ds-DNA is caused by the intercalation of Letrozole to the bulky, slowly diffusing ds-DNA which results in considerable decrease in the surface concentration and apparent diffusion coefficient. According to the data obtained from the plot (figure 8) of i_p(µA) Vs v (mV) the surface concentration (Γ) of the reactant was calculated and the value is 3.1188 x10^{-7}mol^{-1} cm^{-2}. The plot (figure 9) of logarithm of peak current (log i_p) versus logarithm of scan rate (log v) gave a slope of 0.5405.The linear regression equation obtained by plotting log i_p(µA) Vs log v (mV) is,

log i_{pa}(µA) = 0.5405 log v (mVs^{-1}) - 0.2933 ,
R^2 = 0.9511

The decrease in the slope of the linear i_p versus $v^{½}$ plot (R^2 =0.9052), where the slope values are 1.284 and 0.664 mV$^{-1/2}$s$^{-1/2}$ in the absence and presence of ds-DNA respectively and was shown in figure 10. The diffusion coefficient (D_0) of DNA bound Letrozole was found to be 2.2717x10^{-6}cm^{-2}s^{-1} which was lower than the diffusion coefficient of free Letrozole (2.6894 x10^{-6}cm^{-2}s^{-1}). In order to study the rate constant for the heterogeneous electron transfer process, the plot (figure 11) of E_{pa} Vs log $v^{½}$ was used. The linear regression equation obtained was [40, 43]:

E_{pa} (V) = 0.2385 log $v^{½}$ + 0.0722 (R^2 =0.9578)

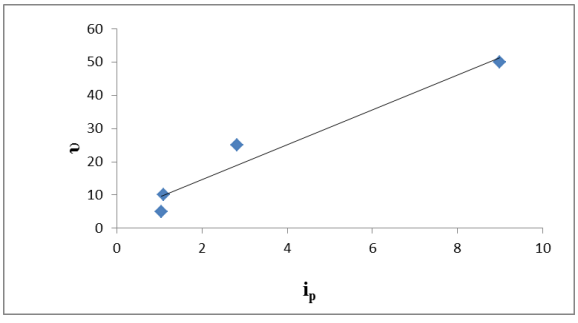


Fig 8: Plot of i_p Vs υ

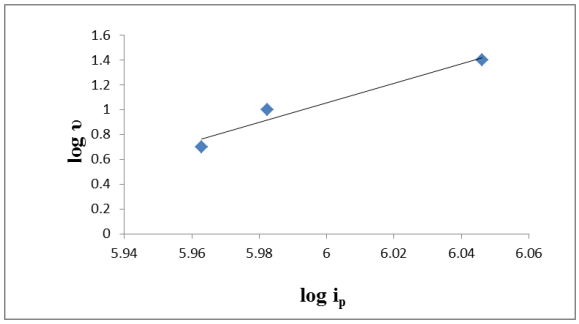


Fig 9: Plot of log i_p Vs log υ

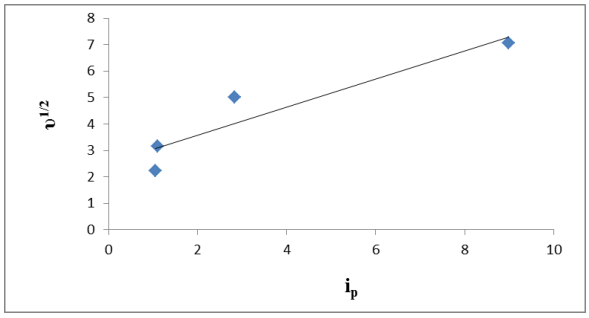


Fig 10 : Plot of i_p Vs $υ^{½}$

The k^0 obtained from the intercept value of the plot of E_{pa} (V) Vs log $v^{1/2}$ was 1.1038 x 10^{-2}cms^1 and this was found to be lower than the k^0 of free Letrozole (1.2320 x10^{-2}cms^{-1}). The changes in current upon addition of ds-DNA can be

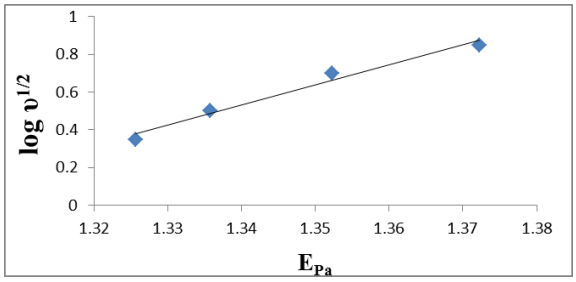


Figure 11 : Plot of E_{pa} Vs log $υ^{½}$

explained in terms of diffusion of an equilibrium mixture of free and bound Letrozole to the electrode and which can be used to quantify the binding of Letrozole to ds-DNA. In this context current titrations were performed by keeping the concentration of Letrozole constant while varying the concentration of ds-DNA using cyclic voltammetry at pH 7.1. The current titration was described by the following equation [44, 45],

log(1/[DNA]) = log K+ log(I_{H-G}/I_G- I_{H-G})

Where, K is the apparent binding constant, I_G and I_{H-G} are the peak current of free guest (G) and the complex(H-G) respectively. Under the assumptions of irreversible, diffusion controlled electron transfer process and a 1:1 association complex between the drug and ds-DNA (in nucleotide phosphate) becomes linear with the intercept of log K

The straight line obtained by plotting (figure 12) log (1/[DNA]) Vs log (I_{H-G}/I_G- I_{H-G}) is ,

log(1/[DNA])= 0.709 log(I_{H-G}/I_G- I_{H-G})+ 5.039, (R^2 =0.988)

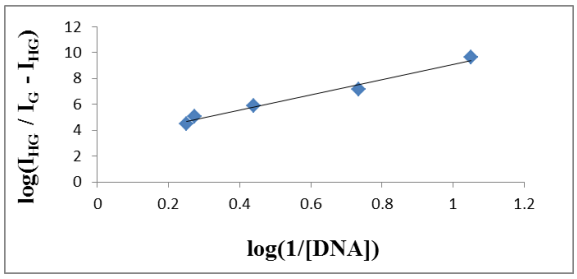


Figure 12 : Plot of log (1/[DNA]) Vs log (I_{H-G}/I_G- I_{H-G})

The binding constant of this complex was evaluated according to the above equation and the result obtained is 1.0939x10^5M^{-1}. The value of K demonstrated that Letrozole binds to ds-DNA with high association constant. The change in Gibbs free energy value (ΔG) for the binding of Letrozole with DNA were calculated from the equation, ΔG = -RTlnK**,** From the K value obtained, the calculated ΔG value for the formation of Letrozole DNA complex is -28.75 KJ mol^{-1}. The negative value of ΔG shows that the binding of Letrozole with DNA is a spontaneous process.

CONCLUSION

Letrozole an anticancer drug was determined using cyclic voltammetric method in this study. The binding of Letrozole with calf thymus ds-DNA was studied and compared with the

binding ability.Cyclic voltammetric studies provide a very low LOD and LOQ values for the determination of Letrozole and show the high sensitivity of the technique. The kinetics of the electrode surface reaction were also studied by calculating the parameters Γ, D and k^0.

ACKNOWLEDGEMENT

The authors are thankful to Head, Chemistry Department, The American College and Head, Chemistry Department, NMSSVN College, Madurai, Tamilnadu, for their encouragement and necessary laboratory facilities.

CONFLICT OF INTEREST STATEMENT

None Declared

REFERENCES

1. Lerman L S. Structural considerations in the interaction of DNA and acridines. J Mol Bio 1957-1961; 3: 18.
2. Waring MJ. The molecular basis of antibiotic action. NewYork, United states: John Wiley and Son; 1972, p 173.
3. Hardman J G, GilmanA G, Limbird L. E. Goodman and Gilman's. The pharmacological basis of therapeutics. New York, NY, USA: McGraw-Hill Companies; 1996.
4. Reszka k, Kolodziejczyk P, Hartley J A, Wilson W D, Lown J W. Anthracycline and anthracenedione based anticancer agents. Amsterdam, Netherlands: Elsevier Press; 1998.
5. Ferrans V J. Overview of cardiac pathology in relation to anthracycline cardio toxicity. Cancer Treat Rep 1978; 62: 955-961.
6. DinorahBarasch, Omer Zipori, Israel Ringel, Isaac Ginsburg, Amram Samuni, Jehoshuan Katzhendler. Novel anthraquinone derivatives with redox-active functional groups capable of producing free radicals by metabolism: are free radicals essential for cytotoxicity? European J Med Chem 1999; 34: 597–615
7. Coldwell K E, Cutts S M, Ognibene T J, Henderson P T, Phillips D R. Detection of adriamycin-dna adducts by accelerator mass spectrometry at clinically relevant adriamycin concentrations. Nucleic Acids Research 2008; 36.
8. Gewirtz D A. A critical evaluation of the mechanisms of action proposed for the antitumor effects of the anthracycline antibiotics adriamycin and daunorubicin. Biochem Pharmacol 1999; 57:727-741.
9. Tewey K M, Rowe T C, Yang L, Halligan B D, Liu L F. Adriamycin-induced DNA damage mediated by mammalian DNA topoisomerase II. Science 1984; 226: 466-468.
10. Gigli M, Doglia S M, Millot J M, Valentini L, Manfait M. Quantitative study of doxorubicin in living cell nuclei by micro spectro fluorometry. Biochimica Biophysica Acta 1988; 950: 13-20.
11. Cummings J, McArdle C S. Studies on the in vivo disposition of adriamycin in human tumours which exhibit different responses to the drug. British J Cancer. 1986; 53:835-838.
12. Terasaki T, Iga T, Sugiyama Y, Sawada Y, Hanano M. Nuclear binding as a determinant of tissue distribution ofadriamycin, daunomycin, adriamycinol, daunorubicinol and actinomycin D. J Pharmacobiodyn 1984; 7:269-277.
13. Fialkoff H, Goodman M F, Seraydarian M W. Differential effect of adriamycin on DNA replicative and repair synthesis in cultured neonatal rat cardiac cells. Cancer Res 1979; 39:1321-1327.
14. Ward D C, Reich E, Goldberg I H. Base specificityin the interaction of polynucleotides with antibiotic drugs. Science 1965; 149: 1259-1263.
15. Calendi E, DiMarco A, Reggiani M, Scarpinate B, Valentini L. On physico-

chemical interactions between daunomycinand nucleic acids. Biochimica Biophysica Acta 1965; 103: 25–49.
16. Pigram WJ, Fuller W, Hamilton LD. Stereochemistry of intercalation: interaction of daunomycin with DNA. Nature: New boil 1972; 235: 17–19.
17. Kawakami Y, Hopfinger A J. Prediction of initial reduction potentials of compounds related to anthracyclines and implications for estimating cardio toxicity. Chem Res Toxicol 1990; 3: 244–247.
18. De Abreu F C, de Ferraz P A L, Goulart MOF. Some applications of electrochemistry in biomedical chemistry, Emphasis on the correlation of electrochemical and bioactive properties. J Brazilian Chem Society 2002; 13: 19-35.
19. Lown J W, Chen H H, Plambeck J A. Further studies on the generation of reactive oxygen species from activated anthracyclines and the relationship to cytotoxic action and cardio toxic effects. Biochem Pharmacol 1982; 31:575–581.
20. Blankespoor R L, Kosters E L, Post A J, Van Meurs D P. Substituent effects upon the peak potentials and reductive cleavage rate constants of hydroxyl and methoxy-substituted 9,10-anthraquinones in 50% aqueous CHCN: do they correlate? J Organic Chem 1991; 56: 1609–1614.
21. Kumbhar A, Padhye S, Ross D. Cytotoxic properties ofiron-hydroxynaphthoquinone complexes in rat hepatocytes. Bio Metals 1996; 9: 235–240.
22. Bartoszek A. Metabolic activation of adriamycin by NADPH-cytochrome P450 reductase; overview of its biological and biochemical effects. Acta Biochimica Polonica 2002; 49:323-331.
23. Das S, Saha A, Mandal P C. Radio sensitization of uracil by Cu(II) and Ni(II) complexes of 1,2 dihydroxy 9,10anthra quinone. J Radio Analyt Nuclear Chem 1996; 196: 57–63.
24. Das S, Saha A, Mandal P C. Radiation-induced doublestrand modification in calf thymus DNA in the presence of 1,2-dihydroxy-9,10-anthraquinone and its Cu(II) complex. Environ Health Perspect 1997; 105:1459-1462.
25. Das S, Mandal P C. Influence of Ni(II) and Fe(III)complexes of 1,2 dihydroxy 9,10 anthraquinone on the modification in calf thymus DNA upon gamma irradiation. Radiation Phys Chem 2009; 78: 37–41.
26. Plambeck JA, Lown J W. Electrochemical studies of antitumor antibiotics. J Electrochem Society 1984; 131: 2556–2563.
27. Parisa S. Dorraji, FahimehJalali. Investigation of the interaction of sertraline with calf thymus DNA by spectroscopic methods. J Braz Chem Soc 2013; 24:6-10.
28. Marmur J. A procedure for the isolation of deoxyribonucleic acid from micro-organisms, J Molecul Biol 1961; 3(2): 208–218.
29. Ali M Abbed, Marwan SM, Al-Nimer Mohammad A, AL hamdany. Effect of chlorpromazine on intact and irradiated aliquot ctds DNA samples. J Fac Med Baghdad 2007; 49(1):157-161.
30. Laura Mora, Karin Y, Chumbimuni Torres, Corbin Clawson, Lucas Hernandez, Liangfang Zhang, Joseph Wang. Real-time electrochemical monitoring of drug release from therapeutic nanoparticles, J Control Release 2009; 140: 69–73.
31. Hajian R, Tavakol M. Interaction of Anticancer Drug Methotrexate with DS-DNA Analyzed by Spectroscopic and Electrochemical Methods. E-J Chem 2012; 9(1): 471-480.
32. Alankar Shrivastava, Vipin B Gupta. Methods for the determination of limit of detection and limit of quantitation of the analytical methods. Chronicles Young Scientists 2011; 2(1):21-25.
33. Burcinbozal palabiyik, Sevinckur Banoglu, Mehmet Gumustas, Bengiuslu, Sibel

Ozkana. Electrochemical approach for the sensitive determination of anticancer drug Epirubicin in pharmaceuticals in the presence of anionic surfactant. Rev Roum Chim 2013; 58(7-8): 647-658.
34. Riley C M, Rosanske T W. Development and Validation of Analytical Methods. New York: Elsevier Science Ltd; 1996.
35. Ozkan SA. Electroanalytical methods in pharmaceutical analysis and their validation. New York: HNB Pub; 2011.
36. Swartz M E, Krull I S. Analytical Method Development and Validation. New York: Marcel Dekker Inc. Pub; 1997.
37. Lund H, Hammerich O. Organic chemistry, 4th edition, New York: Marcel Dekker, Inc. Pub, 2001.
38. Greef R, Peat R, Pletcher L M, Robinson J. Instrumental Methods in Electrochemistry, Chicheste: Ellis Horwood; 1985, p 185.
39. Laviron E, Laviron E, Roullier L, Degrand C. A multilayer model for the study of space distributed redox modified electrodes: Part II. Theory and application of linear potential sweep voltammetry for a simple reaction. J Electroanal Chem Interfac Electrochem 1980; 112 (11):11-23.
40. Shankara S. K, Jaldappagari Seetharamappa, Umesh Katrahalli, Pradeep B. Kandagal. Electrochemical Studies of Buzepide Methiodide and their analytical applications. Int J Electrochem Sci 2008; 3:711-720.
41. Pletcher D, Greff R, Peat R, Peter LM, Robinson J. Instrumental Methods in Electrochemistry. Cambridge: Wood head publishing limited; 2011.
42. Brownson DAC, Banks CE. The Handbook of Graphene Electrochemistry. Verlag London: Springer Ltd; 2014.
43. Elqudaby H M, Gehad G. Mohamed, Ghada MG, El Din. Electrochemical behaviour of trimebutine at activated glassy carbon electrode and its direct determination in urine and pharmaceutics by square wave and differential pulse voltammetry. Int J Electrochem Science 2014; 9: 856–869.
44. Carter MT, Rodriguez M, Bard AJ. Voltammetric studies of the interaction of metal chelates with DNA. 2. Tris-chelated complexes of cobalt(III) and iron(II) with 1,10-phenanthroline and 2,2'-bipyridine. J Am Chem Soc 1989; 111: 8901-8911.
45. Ibrahim MS. Voltammetric studies of the interaction of nogalamycin antitumor drug with DNA. Analytica Chimica Acta 2001; 443 (1): 63-72.

Cite this article as:
Y. Brightson Arul Jacob, J. Jeyasundari. Interaction of Anticancer Drug Letrozole with Ds-DNA Analyzed by Electrochemical Methods. J Pharm Chem Biol Sci 2015; 3(2): 221-229