



Application of DPP for the Determination of Cefdinir in Pharmaceuticals

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The linear range was recognized between 0.875- 7.000 $\mu\text{g.ml}^{-1}$. The calculated results show that LOD and LOQ were equal to 0.3271 and 1.0904 $\mu\text{g.ml}^{-1}$ respectively. This method was successfully applied to assay cefdinir in commercial capsules with 0.089 standard deviation and relative standard deviation less than 2.97 %. The proposed method is simple, accurate, fewer time consuming and even applied without prior separation for the color and excipient solution.

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I. INTRODUCTION

Cefdinir is an extremely beta-lactamase stable third-generation cephalosporin that need been concurred for those medication of a few type of bacterial diseases, chemically known as [(6R,7R)-7-[[[(2Z)-(2-amino-4-thiazolyl)(hydroxylimino) acetyl]amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo [4.2.0]oct-2-ene-2-carboxylic acid], Figure 1^(1,2).

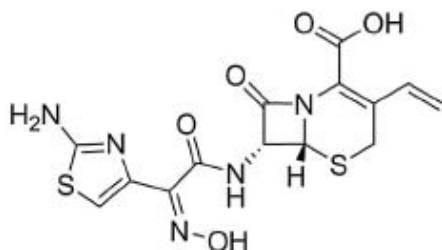


Fig. 1: Chemical structure of Cefdinir

DPP technique was applied for estimation a number of drugs as quality control⁽³⁾. Several analytical needs been describe for those assurance of cefdinir to pharmaceuticals what's all the more living samples. Cefdinir oxidation and reduction voltammetric behavior was studied using hanging mercury dropping electrode HMDE, and glassy carbon electrode GCE versus

Ag/AgCl at pH 4.2 and 5.0 respectively, also a developed adsorptive stripping voltammetric method for cefdinir assay in diverse samples. The results illustrate that linear range among 0.25 to 0.4 μM for HMDE and 0.4 to 10 μM for GCE and the LOQ was 0.2 and 0.26 μM for HMDE and GCE respectively⁽¹⁾.

Direct current polarography, differential pulse polarography and cyclic voltammetry was applied for the cefdinir electrochemical behavior studying at pH ranged from 2 – 12. Diffusion coefficient, transfer coefficient and rate constant as kinetic parameters were calculated. Also the method used for the drug estimation in pharmaceuticals and life tasters⁽²⁾.

New developed spectrophotometric methods for the cefdinir assay in pure sample and pharmaceuticals, in the first, an orange colored complex formed between cefdinir and NQS reagent at pH 11 which analysis at 490 nm while in the second method a yellow colored complex formed between hydrolysis cefdinir with NBD-Cl reagent which analysis at 390 nm. The results show satisfactory accuracy and precision⁽⁴⁾.

A developed first derivative spectrophotometric technique was applied for the assay of cefdinir and cefixime in pharmaceuticals using NaHPO₄ at alkaline solution, pH=8, which measured at 306.8 nm. The results show LOD values was 0.28; 0.45 $\mu\text{g}/\text{ml}$ and LOQ value was 0.98; 1.5 $\mu\text{g}/\text{ml}$ for cefdinir and cefixime respectively⁽⁵⁾.

This study was meant to develop sensitive and simple polarographic method for direct estimation of cefdinir in pharmaceuticals, In addition to, it was intended to examine the reduction behavior of cefdinir on DME electrode, also uncertain reaction mechanisms were proposed.

II. EXPERIMENTAL

a) Apparatus

All polarographic analyses were done with a 797VA Computrace, Metrohm, Herisau, Switzerland which including the three-electrode mode consisted of Dropping Mercury Electrode, DME as working electrode, Ag/AgCl; 3 M KCl as a reference electrode and a Pt auxiliary electrode. pH measurements were get using HANNA pH 211, Microprocessor pH meter, Romania. Distilled water used was obtained from a Water still W4000, Merit. The measurements were carrying out at room temperature $\pm 5^\circ\text{C}$.

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b) Materials and reagents

Every chemicals used were of analytical mark purity and used without additional purification. All the standard, reagents and sample solutions were prepared using distilled water. The cefdinir standard was purchased from Astellas Pharma Inc. Tokyo, Japan. The cefdinir stock solutions ($1000 \mu\text{g}.\text{ml}^{-1}$) were prepared in D.W and stored at less than 4°C . All cefdinir sample solutions were prepared by enough dilution of stock solution. A Sefarin 300mg, pharma international co., Amman, Jordan was selected as commercial pharmaceuticals.

c) Procedure

An aliquot volume of cefdinir sample solutions was pour into a 20 ml polarographic cell. The

voltammetric analyses were carried out after degassing the cell with high purity nitrogen for 5 minutes and then analysis by scanning the potential within the negative direction on DME as working electrode versus Ag/AgCl, 3.0 M KCl as reference electrode and platinum wire as an auxiliary electrode. The final volume in the polarographic cell with all solutions added, cefdinir sample, 0.2 to 0.4ml volume of 3M KNO_3 or 0.5M LiCl as a supporting electrolyte and 2ml Briton-Robinson buffers ^(6, 7) solutions were completed to the 20 ml with distilled water as a solvent, Table-1.

Table-1: The optimum experimental parameters established for cefdinir analysis

Parameters	Conditions value	Parameters	Conditions value
Working electrode	DME	Initial potential	0.00 mV
Supporting electrolyte	KNO_3 or LiCl	Final potential	-1.8 mV
Buffer	B-R, pH 4 and 7	Pulse amplitude	50 mV
Purge gas	99.999% Purity nitrogen	Scan rate	5 mV/sec
Purge time	300 sec	Peak potential	- 0.360 to -0.710 V

d) Preparation of commercial Cefdinir

Cefdinir 300mg capsules were get from a local pharmacy in Baghdad and used as a dosage form. Two capsules each one contains 300 mg cefdinir were mixed well and homogeneous then an accurate weighed sample was transferred into a 50 ml volumetric flask containing 10 ml of distilled water. The solution inside the volumetric flask were shakes severely for few minutes and the volume of this flask was completed to the total volume using D.W, then this solution was filtered and the clear solution was used to prepare the like concentration for the analysis.

III. RESULTS & DISCUSSION

a) pH effect

The DPP reduction polarogram of cefdinir at the optimal experimental conditions showed one clear and more sensitive reduction peak at applied potential ranging from -0.5 to - 0.95 V with other slight sensitive peaks.

The peak current of cefdinir at pH values, 4, 7 and 9 showed more negative $E_{1/2}$ voltage when the acidity lessen, Figure 2, therefore, at the alkaline solution, a little proton ion involvement, the reduction process isn't simply facilitate compared with neutral and acidic media, ^(8, 9) also the results show an relative decreasing in the peak intensity and sensitivity in alkaline media, this results confirm that the reduction reaction engage the protons and the cefdinir electrochemical activities depends on the pH.

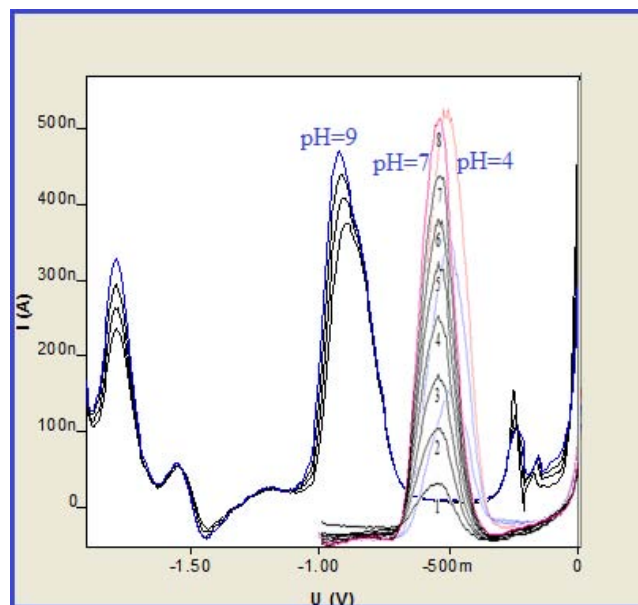


Figure 2: DPP polarograms for cefdinir solutions at pH 4,7 and 9

b) Calibration plot

For the determination of cefdinir, a standard calibration plot of cefdinir was prepared and applied using the Least Squares Method, LSM ⁽¹⁰⁾ in the concentration range $0.875\text{--}7.000 \mu\text{g}.\text{ml}^{-1}$ using DPP on DME in Britton-Robinson buffer at pH 4 and 7 also 0.06M KNO_3 and 0.01M LiCl. One reduction peak has height greatness and sensitivity in - 0.518v was observed and chooses. The peak current i_p was proportional to the concentration, Figs.3 and 4. The accuracy and precision of the method was tested, the

results showed the SD was 2.14 and LOD and LOQ was 0.3271 and $1.09 \mu\text{g.ml}^{-1}$ respectively, the regression equation and correlation coefficient, r , and other analytical merit number⁽¹⁰⁾ were summarized in Table-2.

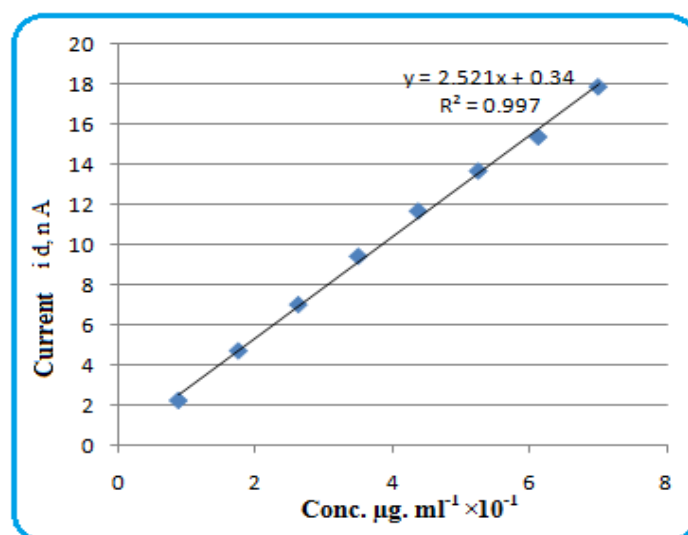


Figure 3: Calibration curves for the determination of cefdinir using DPP at optimal conditions

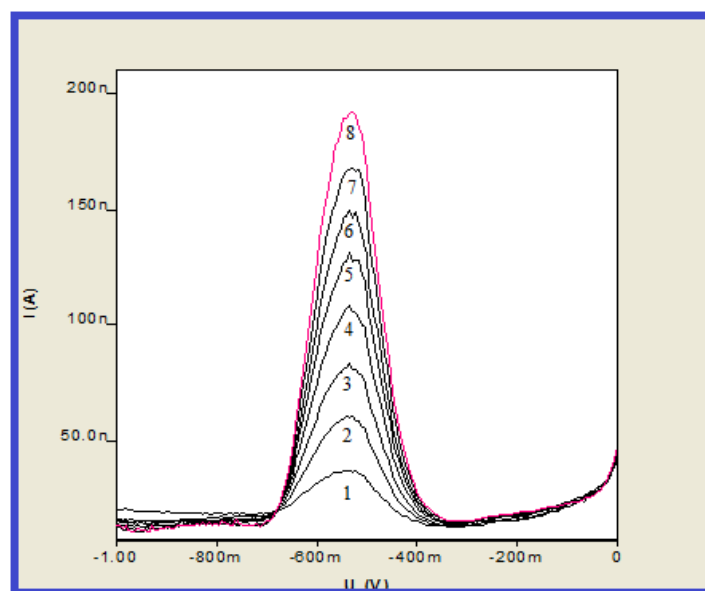


Figure 4: The DPP polarograms of cefdinir at optimum conditions in pH= 4 and B-R buffer at concentrations range 0.875 to $7.0 \mu\text{g.ml}^{-1}$

Table-2: Analytical merit number for the assaying of cefdinir by suggested DPP method

Parameters	Values	Parameters	Values
Regression equation	$\text{id} = 2.521 X + 0.34$	Random errors in the Y direction, $S_{y/x}$	0.2749
Concentration range, $\mu\text{g.ml}^{-1}$	0.875 to 7.000	Standard deviation of slope, S_b	0.0485
Slope of the line, b	2.521	Standard deviation of intercept, S_a	0.214
Intercept, a	+ 0.34	C.L. for the slope ($b \pm t_{(n-2)} S_b$) at 95%	2.521 ± 0.1188
Correlation coefficient, r	0.9984	C.L. for the intercept ($a \pm t_{(n-2)} S_a$) at 95%	0.34 ± 0.524
Coefficient of determination, R^2	0.9968	LOD 3.3 SD, $\mu\text{g.ml}^{-1}$	0.3271
Standard deviation, SD	2.14	LOQ 10 SD, $\mu\text{g.ml}^{-1}$	1.09

c) Applications

The accuracy, precision and repeatability of the method was experienced by deference measurements

for 3 and $5 \mu\text{g.ml}^{-1}$ synthetic cefdinir samples, the amounts found to be 3.06 ± 0.13 and 5.09 ± 0.23 and the relative error ranged between -1 to +4.3 and -0.98 to

+4.52, also the results show suitable and accurate values for standard error of the mean and the confidence limit of the mean, Table-3.

Table-3: Determination of cefdinir in synthetic sample in B-R buffer at pH 4

Initial Conc. $\mu\text{g.ml}^{-1}$	Calculated Conc., av. $\mu\text{g.ml}^{-1}$	SD	RSD	Absolute Error, Range	%Relative Error	Standard Error of the mean	Confidence limit of the mean
3.00	3.06	0.089	2.97	-0.03 to +0.13	-1 to +4.3	0.036	3.06 ± 0.0934
5.00	5.09	0.13	2.55	-0.08 to +0.23	-0.98 to +4.52	0.32	5.09 ± 0.136

$n=6, t= 2.57$

The application for the cefdinir determination in commercial pharmaceuticals using DPP on DME in B-R buffer at pH 4 in 0.06M KNO_3 or 0.01M LiCl, the result shows that the absolute error ranged within the 0.08 to

+0.17 and the relative error don't exceed 2.8%, Table-4, the results prove that method has accepted precision and repeatability.

Table-4: Determination of cefdinir in pharmaceutical sample in B-R buffer at pH 4

Initial Conc. $\mu\text{g.ml}^{-1}$	Calculated Conc., av. $\mu\text{g.ml}^{-1}$	SD	RSD	Absolute Error, Range	%Relative Error	Standard Error of the mean	Confidence limit of the mean
6.00	6.11	0.1	1.62	-0.08 to +0.17	-1.3 to + 2.8	0.045	6.11 ± 0.124

$n=5, t=2.78$

e) *Electro-chemical activities and number of electrons*

The ilkovic-Heyrovsky equation describes the entire current – potential curve and calculates the number of shared electrons in the electrode process of a reversible redox system in polarography.

$$E = E_{1/2} + \frac{RT}{nF} \ln \left(\frac{i_d - i}{i} \right)$$

Where i_d is the diffusion current and i is the current at these points of the polarographic stage which corresponding to the applied potential E , and $E_{1/2}$ is the half-Wave potential, ^(8, 9, 11) hence by plotting applied potential, E against $\log\{(i_d - i) / i\}$, a straight line is obtained which present that the electrode process is reversible in these case that the slope of the line indicated the values of n , i.e. the number of electrons transferred in the electrode reaction in view to the wave reversibility, when the number of electrons was integers numbers, it's refers to reversible electrochemical process, whereas the rational number refers to irreversible electrochemical process ^(12, 13). The calculated value of the $E_{1/2}$ was -0.504V and 4 electrons really required for the reduction, Figure 5, thereby, depending on the number of electrons obtained and $E_{1/2}$, the choicest planned reduction mechanism recommended that the azomethine group gets reduce to the saturated amine group via actually four electrons process at reversible electrochemical process, this reduction takes place at neutral and alkaline solution and at about -0.4v, reaction A, while the preferred reduction mechanism in acidic solution recommended reduce the azomethine group to the ammonium ion, reaction B, owing to the

presence concentration of protons participation appear to make the reduction easier allowed to form ammonium salt, Figure 6 ^(8, 14).

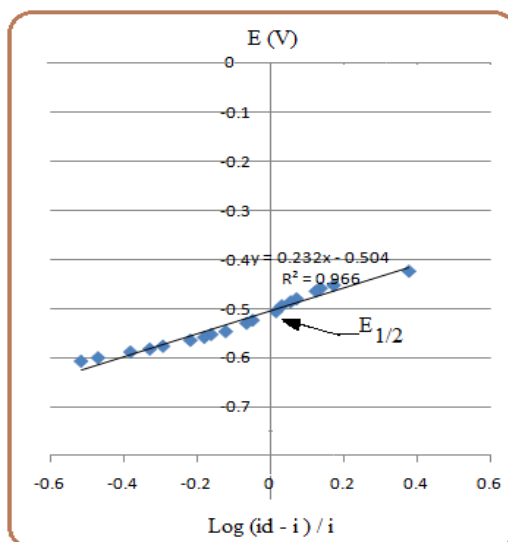


Figure 5: The relation between the potential E and the logarithms of $\{ (i-d) / i \}$ for cefdinir

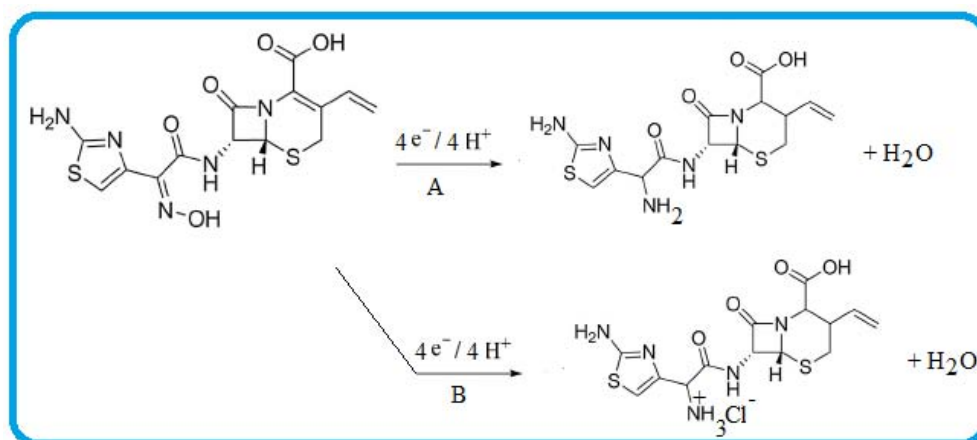


Figure 6: Optional and expect reduction mechanism of cefdinir

IV. CONCLUSION

The electro-chemical reduction activities and analysis of the cefdinir drug in B-R buffer over a pH range of 4-9 was studied. The participation proton appear to make the reduction easier, other than in basic media, the reduction route isn't make easy due to the non-availability of protons ⁽¹²⁾. The statistics results confirm that DPP is one of the finest analytical apparatus for drugs estimations, more, this technique is sensitive, accurate and needed a fewer time also, it's used without prior separation for color and excipient samples before the analysis.

REFERENCES RÉFÉRENCES REFERENCIAS

1. Ibrahim H.T. (2014) Electrochemistry and determination of cefdinir by voltammetric and computational approaches, Journal of Food and Drug Analysis 22, 527-536.
2. M.V. Narasimha, G.V.Subba Reddy (2012) Electrochemical reduction behavior and analysis of cefdinir in pharmaceutical formulations and biological media. African Journal of Scientific Research 7 (1), 364-377.
3. Salam A.H. Al-Ameri¹, Mohammed D. Majeed AL-Mayahi (2016) A highly sensitive electrochemical determination of Isoniazid in pharmaceutical preparation by differential pulse polarography. Int. J. of Chem. Eng. Res. 3 (5), 9-15.
4. A. A. Gouda, H. Hashem; W. Hassan (2011) Spectrophotometric methods for determination of cefdinir in pharmaceutical formulations via derivatization with 1,2-naphthoquinone-4-sulfonate and 4-chloro-7-nitrobenzo-2-oxa-1,3-diazole. Drug Testing and Analysis, John Wiley & Sons. Ltd.
5. Erhan B., Serap O., Mehmet G., Ismail M. and Feyyaz O. (2013) First derivative spectrophotometric determination of cefixime and cefdinir in pharmaceutical preparations. Turk. J. Pharm. Sci. 10 (3), 321-328.
6. Lastra O.C., Igor H.J., Hugo J.S., Renato F.P. (2003) Development and validation of an UV derivative

spectrophotometric determination of Losartan potassium in tablets. J. of Parma. and Biomed. Anal. 33(2), 175-180.

7. Chandra M. (2003) Buffers, CALBIOCHEM, EMD Biosciences, Inc. Darmstadt, Germany.
8. Zuman P.(1970) Topic in organic polarography", Plenum Press, London, New York, pp 40-52.
9. Joseph Wang (2000) Analytical Electrochemistry. John Wiley & Sons, INC., Pp64, 2nd Ed.
10. James N.M. & Jane C.M.(2005) Statistics and chemometrics for analytical chemistry, Pearson Education Limited, Prentice Hall, 5th Ed.
11. Salam A.H. Al-Ameri¹ & Najlah M.H. Al-Waeli.(2016) Differential Pulse Polarographic Study of Amoxicillin and Ciprofloxacin and its Determination in Pharmaceuticals, International Journal of Bio Analytical Methods & Bio Equivalence Studies, IJBMS 3(1), 47-54.
12. Elham Al-Rufaie; Mohamed A.K. H.(2014) Study of interaction between vitamin C and Nickel II ion using a polarographic methods. Iraqi J. of Science 14, No3A, 878-885.
13. Najdat R.H. AL – khafaji (2014) Thermodynamic and Kinetic Studies on the effectiveness of Nutritional origin Poly Phenols in Lead Poisoning protection, PhD Thesis, College of Science University of Baghdad, pp 114-118.
14. Henning Lund (1959) Electro-organic preparations: VI. Reduction of compounds containing the Azomethine group, Acta Chem. Scand. 13, No.2, 249-267.