ISSN: 0974-5823 Vol. 7 No. 2 February, 2022

International Journal of Mechanical Engineering

Electrochemical Determination of Manidipine Dihydrochloride in a Pharmaceutical Preparation Using Carbon Paste Electrode

Hassan A.M. Hendawy[1], Alaa S. Amin[2], S. M. N. Moalla[3], and Mai Aish[3]

National Organization for Drug Control and Research (NODCAR), 6 Abu Hazem Street, Pyramids Ave, P.O. Box 29, Cairo, Egypt

[1]Department Chemistry, Faculty of science Benha University, Benha, Egypt

[2]Department Chemistry, Faculty of science, Port Said University, Port Said, Egypt.

[3]Department Chemistry, Faculty of science, Port Said University, Port Said, Egypt

Abstract - On the basis of the improved electrochemical response at an electrode made of carbon paste ,a precise voltammetric determination for Manidipine biological fluids and pharmaceutical preparations has been investigated. For achieve purpose to analyze MAN in 0.05 M universal buffer (pH=4.2), the electrode made of carbon paste provides voltammetric with good stability, sensitivity and a broad range of application. The Square wave technique shows linearity across the quantification limit and also detection limit values that have been considered to be 0.72 and 0.16 µg/ml. For the purpose to determine Manidipine in pharmaceutical preparations, there has also been a statistical validity comparison with the published approach.

Index Terms - Voltammetric technique, Cyclic voltammetric technique, Manidipine Dihydrochloride, electrode made of carbon paste, Square wave voltammetric technique

INTRODUCTION

Manidipine Dihydrochloride (MAN) is a dihydro-2,6-dimethyl4(3-nitrophenyl)-3,5-pyridine dicarboxylic acid is 1,4-dihydro-2,6-dimethyl4(3-nitrophenyl)-3,5-pyridine dicarboxylic acid and also act as Antihypertensive and vasodilator calcium antagonist drug [1-2] in **Fig 1**. A survey of the literature indicated a spectrophotometry [3] and a few high performance liquid chromatography (HPLC) methods to determine Manidipine Dihydrochloride in bio-fluids [4-6]. additionally, no high-performance liquid chromatographic methods to determinine Manidipine in bulk and preparations as a stability indicating test method have been discovered.

Because there is currently insufficient information on the electrical response of Manidipine in pharmaceutical preparation, we utilized Cyclic Voltammetry (CV) and Square wave voltammetric technique (SWV) to establish the electrical behaviour of MAN in pharmaceutical preparations. considering that the design of high-performance liquid chromatographic technique (HPLC) to determinine manidipine in biological fluids using the column-switching technique and ultra-violet identification in 1989 [7], These approaches, however, were insufficiently sensitive for manidipine pharmacokinetic study.

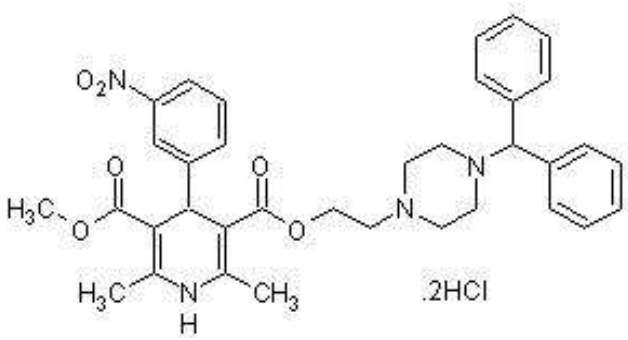


Figure 1. Chemical structure of Manidipine HCl.

Although the published methods are sensitive enough to detect nano-molar levels, the popular of them employ electrodes, that are risky to the environment, and the rest use high-priced electrodes. As a result, cost-effective, and sensitive approach for determining Manidipine in pharmaceutical formulations is required. This study uses an electrode made of carbon paste (CPE) to determine MAN in tablet samples using SWV and CV.

MATERIALS AND METHODS

APPARATUS

Voltammetric measurements have been accomplished utilizing Metrohm797 VA Processor and three electrodes: reference electrode of Ag/AgCl/saturated KCl, working electrode and also auxiliary electrode of a wire made of platinum. At room temperature, all measurements were taken.

The buffer solution was prepared using a pH-meter Orion-Research moder 601 A/Digital Ionalyzer with a glass combination electrode and calibrated using standard buffers at ambient temperature.

Micropipette (Eppendorf-multipipettes plus) was employed in this study.

I. Procedure

Standard Solution Preparation.

All reagents utilized were of pharmacopoeia grade purity and water was bidistilled. Manidipine Hydrochloride was gladly provided by (NODCAR) (99.80 %). Stock solutions of 10^{-2} M were made by dissolving a suitable amount of Manidipine Hydrochloride in 25ml Methanol and completing the solutions to (100 ml) with the same solvent. (BR) buffer solutions (2.0-10) As an electrolyte, 0.05 M in CH_3COOH, ortho-phosphoric, and $B(OH)_3$ acids, and the pH of the acids adjusted to 2.0 utilizing a sodium hydroxide solution [8].

II. Pharmaceutical Tablet Samples preparation.

Carefully, grind ten tablets of KERDICA 20 substance. To produce the desired concentration of MAN, a suitably adequate portion of tiny powder was taken as equivalent to MAN's Stock solution and transferred to a 100 ml measuring flask and supplemented with a suitable electrolyte buffer to the required volume. contents of the beaker were sonicated for 30 minutes to accomplish totally separation and to prepare varying concentrations and transfer it to applicable portions of the fluctuating solution, the process was carried out by following the methods above [9].

III. Spiked urine analysis

Mixing of an aliquot (1 ml) of the pure solution with 15 ml of BR and finally spiked with 10^{-3} M of MAN then follows the procedure below.

IV. Working Electrode preparation.

The electrode made of carbon paste preparing by polishing its surface with aqueous slurry of Before every electrochemical exponent, apply alumina powder on a polishing cloth.Then, it was cautiously washed with ethanol and bidistilled water, and softly dried in the air [10].

V. Method of Analysis.

A square wave voltammetry in the range of +50 to +125 mV was used to determine the quantitative concentration of MAN utilizing an electrode made of carbon paste as a working electrode. The electrochemical response of standard manidipine at an electrode made of carbon paste was examined using CV in the potential range of +0.5 to +1.2 V. Using cyclic voltammetry, the effects of a scan rate of 0.95-1.75 V/**s** and a pH of 2 to 10 on the peak potential and peak current of manidipine have been examined

RESULTS AND DISCUSSION

Manidipine Cyclic Voltammetric Analysis at CPE

Cyclic voltammograms of 0.01 M of MAN were verified in 0.05M B-R buffer solution (pH 4.2) at 100 mV/s as a scan rate by using CPE and revealed a sharp single anodic peak at roughly 1.10 V in **Fig 2**.

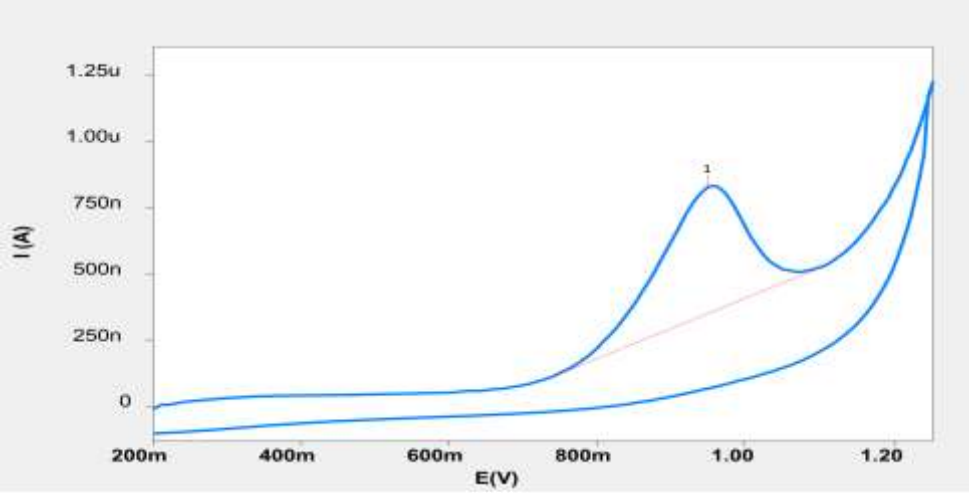


Figure 2. Cyclic voltammogram of Manidipine HCl 0.01 M in BR buffer (pH 4.2) at 100 mV/s as a scan rate at CPE.

I. The Scan Rate parameter on The Oxidation of MAN

The influence of scan rate on MAN oxidation was examined by recording voltammograms of a 1.5 µg/ml MAN solution in BR buffer solutions (0.05 M of pH 4.2, example CV curves of MAN at variety of the scan rates are given in **Fig 3**. The scan rate investigations were performed to see if the process done on the selected electrodes was regulated by diffusion or adsorption. Using CV, the scan rate effect on the peak current and potential was investigated over the scan range 0.95-1.75 V/s, revealing that the peak of the current rose while the peak potential remained unchanged as the scan rate was raised. putting Ipa vs. log v resulted in a straight line with a slope near to 0.48 in the case of CPE, which is indicated to an unique reaction of electrode diffusion process.

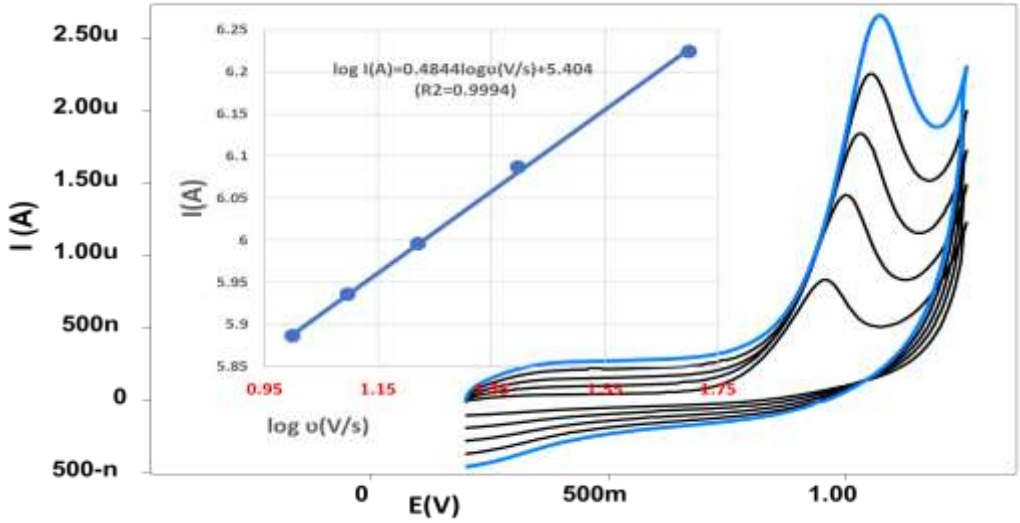


Figure 3. Cyclic voltammograms of (1.5 µg/ml) MAN in 0.05M B-R buffer (pH 4.2) with various scan rates (0.95-1.75 V/s).

throughout the scan range 0.95-1.75 V/s, revealing that the peak current rose as the scan rate raised. In the instance of CPE, putting Ipa vs. log v yielded a straightforward line with a strong correspondence (R^2= 0.9994), which is represented for a perfect response of diffusion-controlled electrode processes,The number of electrons (n) exchanged during the electro-oxidation of MAN was also calculated to be 1 by using the laviron equation [11].

II. The pH Effect on The Electrolyte

The voltammetric response of MAN was examined in the pH range 2–10 in **Fig 4**. At pH 4.2, the maximum current response was obtained. So, this pH was chosen as the best. As a result, a four-electron and four-proton reaction mechanism was proposed **(Scheme1)**. The loss of high electron density linked with the nitrogen atom is differentiated in the molecular orbital computation by several processes such as MMF94 and MOPAC utilizing chemoffice 2017 software.

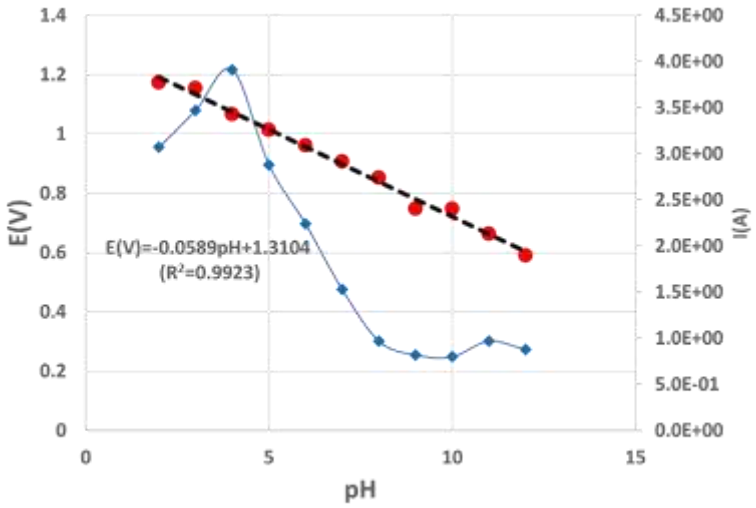
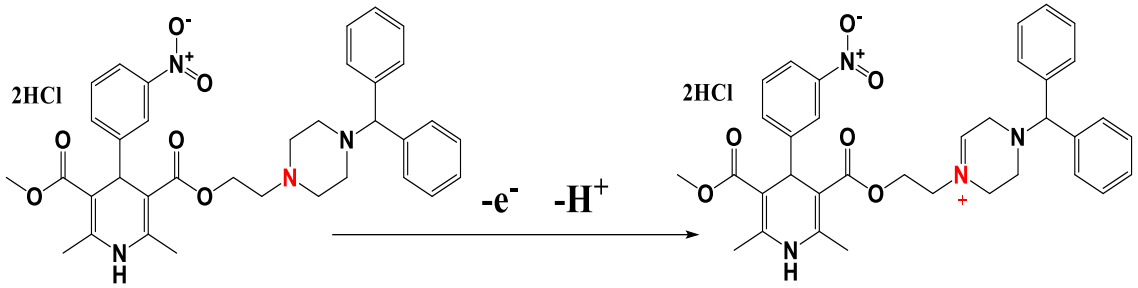


Figure 4. The effect of pH on the anodic current peak and potential behaviour for 1.5 µg/ml Manidipine HCl at CPE at 100 mv/s.



Scheme 1. Tentative Scheme for the oxidation reaction of MAN at CBE.

Quantitative Determination of Manidipine in Pharmaceutical Formulation.

The square wave voltammograms of CPE in pH= 4.2 (BR) solution containing no MAN (a) and 0.01 M MAN are shown in **Fig 5**. (b). As may be observed in the image, in the buffer solution that contains no MAN (curve (a) in Figure 5), there is no peak at CPE. In a pH 4.2 B-R solution containing 1 M MAN, however, the identical working electrode produced a stronger oxidative peak (curve (b) in Figure 5).

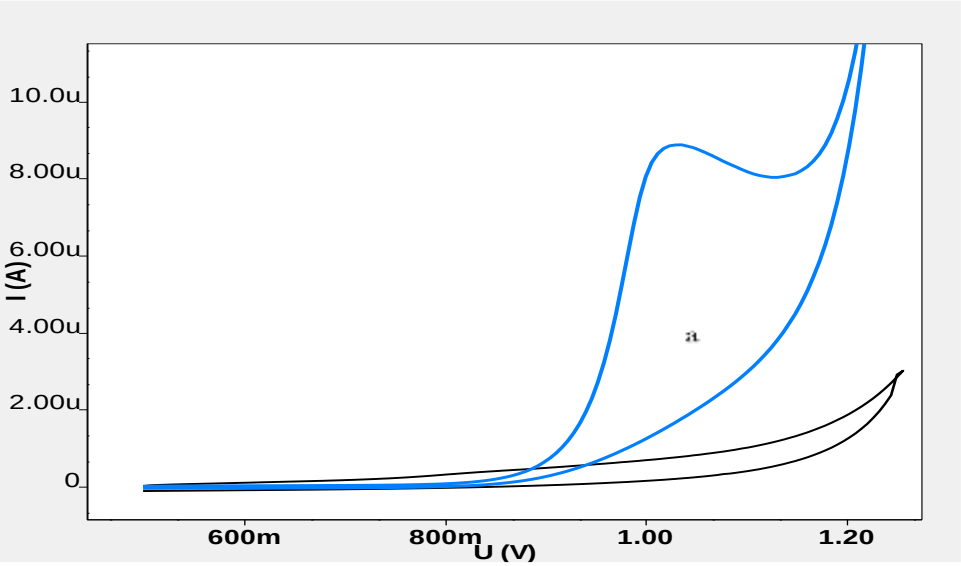


Figure 5. Square Wave Voltammograms of CPE in 0.05M (BR) buffer solutions with (a) no MAN and (b) 0.01 M MAN.

III. Validity of the method

the SWV method was chosen to develop a voltammetric procedure for drug quantification because the peaks were more pronounced and distinct in the decreasing of MAN concentrations than those obtained by measuring SWV with negligible charging current, improving accuracy. The proposed technique's validity was assessed by comparing it to the following ICH guidelines: robustness, precision, linearity, accuracy, LOD, specificity, LOQ [12].

IV. Linearity

the experimental conditions which studied (accumulation potential, pH , SWV frequency, step potential amplitude, accumulation time and of (+8.6 mV, 4.2, 10 Hz, 5.951 mV, 19.99 mV, 5s ,respectively), The correlation between square wave voltammetric peak current and concentration of MAN and the applicability of the method were examined in the range 1.24-12.61 µg/ml. voltammograms of the square wave of various concentrations of MAN, adjusted for background, are shown in **Fig 6**, also containing the inset. Utilizing the below equations, LOQ and LOD have been considered to be 0.72 and 0.16 µg/ml, respectively.

$$LOD = (3.3\ \sigma)/\ S \qquad LOQ = (10\ \sigma)/\ S$$

There has been a good association with the regression coefficients obtained from the results computed to ICH guidelines [13, 14] as appeared in Table (1).

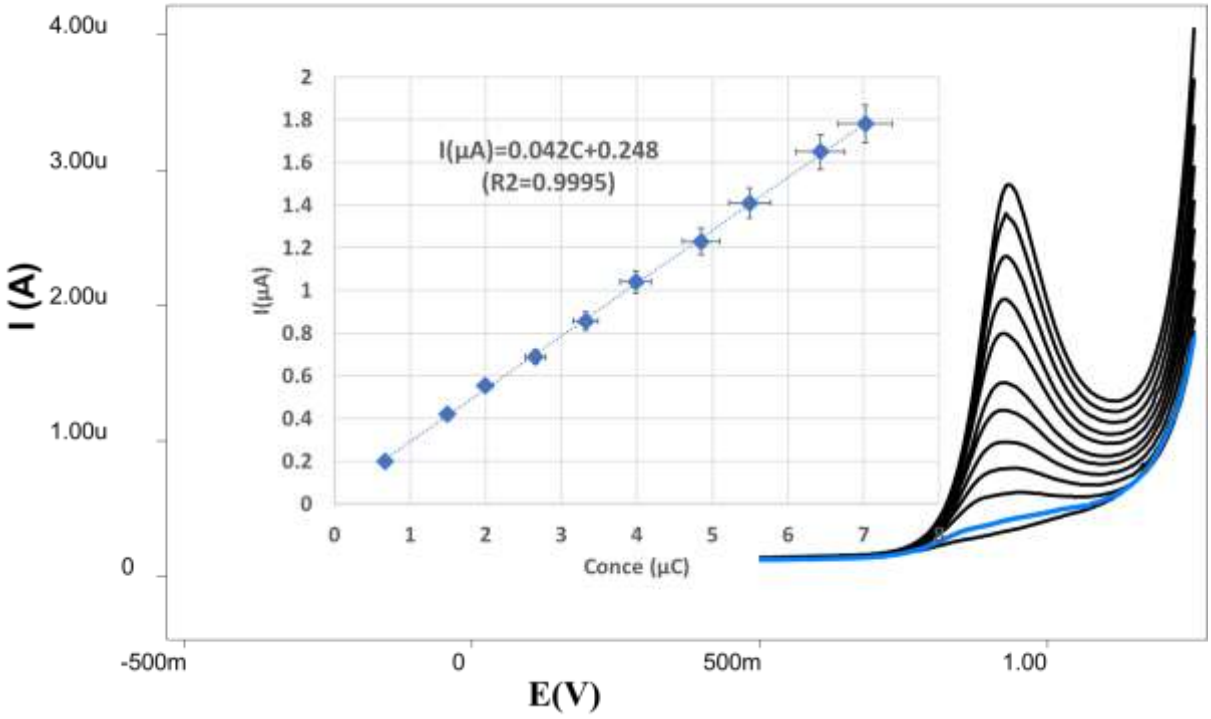


Figure 6. Voltammograms of the Square-wave for linear concentration of Manidipine HCl in B-R (pH 4.2) (0.05 M) with frequency=10 Hz, amplitude =19.9 mV, Voltage step=5.951 mV.

V. Precision

Precision was tested throughout the day and between days by analyzing freshly generated samples in triplicate measurements on one day and a different day [15], using the investigated technique on each day. Examination of the SWV process by utilizing The inter-day method and intra-day method of the data attained, and there was no significant change in the voltammetric signal in the concentration range tested, indicating that the proposed procedure had a perfect accuracy and precision, as shown in Table 1.

VI. Robustness

The robustness of techniques examines a method's viability without being impacted by minor variations in ideal parameters that occur during measurements without impacting the method's results [16, 17]. With minor adjustments in the experimental setting, the robustness of the current approach suggested by the response current wave stability was proven. Her research criteria included pH deviation (± 0.1), equilibrium duration in each volttametric measurement (12 ± 5 s). the significant fluctuations that may occur during the measurement technique wouldn't alter the peak current maximum of the MAN, so the suggested approach has more been consistent than the reported procedure.

VII. Specificity

The peculiarity of the SWV method was confirmed through its capability to measure of MAN in the medical form without interfering resulted from preservatives and excipients that are often present in the pharmaceutical form as listed in **Table (2).**

VIII. Application

The recommended procedure has been employed productively for quantitative measurement of MAN in formulations to validate the applicability of the CPE electrode for analysis of actual samples. It's possible that some of the quantitative matrix measurements were done using the conventional addition approach to reduce the effect. **Table (2)** shows the results of the computations. As a result, the differences in display obtained using the reported approach [18] are not significant.

CONCLUSION

The current research presents a novel surface modified CPE schematic and it has been applied to quantitative measurement of MAN. MAN detection at carbon paste electrode offers a precise technique, where the voltammetric oxidation behaviour of MAN appears to be a single anodic peak, through a SWV voltammetric determination of MAN in pure, dosage forms, and biological fluid. The current process has various advantages, including high sensitivity, and consistency, and these voltammetry methods have several advantages, including low detection limits and applicability for drug evalution in laboratories for quality

control. The new method was compared to the reported method and found to be an exact, straightforward, and sensitive method for quantifying MAN.

Table 1. Validity for SWV determination of MAN on CPE.

Parameters*	Sensor CPE
Linearity rang (µg/ml)	1.24-12.61
Intercept	0.248
Slope	0.042
SD of intercept	0.01
SD of slope	0.001
Multiple R	0.9998
R Square	0.9995
Standard Error	0.014
RSD%	0.82
LOD (µg/ml)	0.16
LOQ (µg/ml)	0.72
The peak current Repeatability (RSD %)	0.64
The peak current Reproducibility (RSD %)	1.11
The peak potential Repeatability (RSD %)	1.05
The peak potential Reproducibility (RSD %)	0.781

Statistical calculations were accomplished utilizing Excel 2020 with one-way analysis of variance (ANOVA).

SD=standard deviation, r = correlation coefficient; r^2 = coefficient of determination.

Table 2. MAN Determination in formulation, and urine samples utilizing CPE.

sample	Added (µM)	Found (µM)	Bais %	Recovery (%)	HPLC*
Tablet	0.1	0.101	0.1	101	99.96
	0.4	0.397	0.3	99.25	100.2
	0.8	0.81	1	101.25	98.97
Mean				100.50	99.71
Variance				1.19	0.43
F-test					2.79
F-tabulated					19
t-test					1.08
t-tabulated					2.78
Spiked urine	0.1	0.101	0.901	101	99.95
	0.4	0.398	0.595	100.75	99.97
	0.8	0.795	0.194	99.38	101.01
Mean				100.33	100.31
Variance				0.40	0.37
F-test					1.08
t-test					0.05

- Every result is the average of three individual assessments, the tabulated t and the variance radio test values at P=. (0.05).

REFERENCES

[1] S.M. Cheer, K. McClellan, Manidipine, Drugs, 61 (2001) 1777-1799.

[2] K. McKeage, L.J. Scott, Manidipine, Drugs, 64 (2004) 1923-1940.

[3] A. Roca-Cusachs, F. Triposkiadis, Antihypertensive Effect of Manidipine, Drugs, 65 (2005) 11-19.

[4] L. Sivasubramanian, K. Manikandan, M. Venkatesan, K.J.J.o.Y.P. Lakshmi, Quantitative analysis of manidipine dihydrochloride in bulk and synthetic mixtures by visible spectrophotometry, 1 (2009) 175.

[5] N. De Laurentis, V. Losacco, M. Milillo, A.J.B.c.f. Zarrilli, Spectrophotometric determination of manidipine dihydrochloride based on formation of charge-transfer complex with iodine, 140 (2001) 15-19.

[6] G. Ragno, F. Aiello, A. Garofalo, G. Ioele, M.S.J.I.F. Sinicropi, Multivariate least squares regression applied to the spectrophotometric analysis of manidipine and its main photoproduct, 58 (2003) 909-915.

[7] V. Todeschini, M. da Silva Sangoi, N.M.J.E.J.o.M.S. Volpato, Delapril and Manidipine Measurements by Liquid Chromatography—Tandem Mass Spectrometry in a Pharmaceutical Formulation, 17 (2011) 287-296.

[8] H.T.S. Britton, R.A. Robinson, Journal of the Chemical Society (Resumed), (1931) 1456-1462.

[9] H.A. Hendawy, W.M. Salem, M.S. Abd-Elmonem, E.J.J.o.a.m.i.c. Khaled, Nanomaterial based carbon paste electrodes for voltammetric determination of naproxen in presence of its degradation products, 2019 (2019).

[10] Z. Tunay, I. S¸ahin, and N. Nakiboglu, "Voltammetric determination of boron using cobalt phthalocyanine modified carbon paste electrode," International Journal of Electrochemical Science, vol. 6, no. 12, pp. 6628–6638, 2011.

[11] C. M. A. Brett and A. M. O. Brett, Electrochemistry Principles, Methods, and Applications, Oxford University Press, Oxford, UK, 1st edition, 1993.

[12] Q.T.Z.J.L.S.I. Ma, Determination of Residual Organic Solvent in Manidipine Hydrochlorideby Solution Headspace Gas Chromatography [J], 2 (2006).

[13] J.M.J.A.c. Green, Peer reviewed: a practical guide to analytical method validation, 68 (1996) 305A-309A.

[14] E. Rozet, A. Ceccato, C. Hubert, E. Ziemons, R. Oprean, S. Rudaz, B. Boulanger, P.J.J.o.C.A. Hubert, Analysis of recent pharmaceutical regulatory documents on analytical method validation, 1158 (2007) 111-125.

[15] S. Chandran, R.J.D.P.-A.I.J.o.P.S. Singh, Comparison of various international guidelines for analytical method validation, 62 (2007) 4-14.

[16] I. Taverniers, E. Van Bockstaele, M.J.P.S.E.D.D. De Loose, Development, Manufacturing, Analytical method validation and quality assurance, (2010) 1-48.

[17] S.L. Karunanidhi, L. Sivasubramanian, M.J.E.J.o.C. Krishnan, Stability indicating HPTLC method for quantitative estimation of manidipine sihydrochloride API, 2 (2011) 113-116.

[18] P.C. Meier, R.E. Zünd, Statistical methods in analytical chemistry, John Wiley & Sons2005.