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Cyclic Voltammetric determination of 1, 4-Dihydro pyridine drugs using MWCNTs modified glassy carbon electrode

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ABSTRACT

MWCNTs are believed to be favorable for the oxidation of electroactive species towards cathodic direction with the simultaneous enhancement of the peak current. The prepared electrode showed an excellent electrocatalytic activity towards the oxidation of antihypertensive drugs leading to a marked improvement in sensitivity. The MWCNTs-modified GCE exhibited a sharp anodic peak around 0.6 V peak potential for Lercanidipine (LERD) and 0.4 V peak potential for Nifedipine (NIFD) in the cyclic voltammograms. The antihypertensive drugs were determined by using a simple two-step procedure developed which comprised a preconcentration step followed by the differential pulse voltammetric quantification. Concentration calibrations were linear within the range from 0.02 to 0.3 μg /mL for LERD and 0.025 to 0.3 μg /mL for NIFD. The lower limits detection (LOD) was found to be very low on modified electrode. An electrochemical sensor featuring the MWCNTs-modified electrode was applied successfully for the 1, 4-dihydropyridines determination in pharmacutical samples.

Key words: Lercanidipine, Nifedipine, Electrochemical, Multiwall carbon nano tubes, Cyclicvoltammetry.

INTRODUCTION

Calcium channel blocker belonging to the 1,,4-dihydropyridine family has commonly been used as a potent arterial vasodilator in the management of angina and cardiovascular diseases [1]. Electrochemistry plays an important role to study the formation of radical and its reactivity in one-pot systems [2, 3]. There are several reports in literature concerning the development of stable CNT-based electrodes for environmental samples, electrochemical sensors, electrocatalysis and for electrochemical estimation of drugs and compounds of biological interest [4, 5]. However, simple but effective method for the development of homogeneously and stably assembled CNT-based electrode is particularly desired for electroanalytical determinations. MWCNTs-based electrodes were prepared generally by casting MWCNTs suspension on conventional electrode surface [6, 7]. The resulting electrodes have been successfully utilized in the sensitive detection of various biological molecules such as uric acid [4], folic acid [6] and cytochromec [7]. Generally, MWCNTs-based electrodes enhance the detection sensitivity and improve reversibility as it can promote electron transfer [8].

An important milestone in the history of carbon is the discovery of carbon nanotubes (CNTs) [9] having two distinct types of structures namely single walled and multiwalled. As a consequence of the excellent electronic and conducting properties of CNTs, electrodes modified with CNTs have demonstrated to improve the electroanalytical performance of different species. Due to their uniqueness, CNTs have received enormous attention for the preparation of electrochemical sensors as it was extensively reviewed [10-15]. The subtle electronic behavior of

CNTs reveals that they have the ability to promote electron-transfer reaction when used as electrode materials. Recently CNT film coated electrodes have received increasing attention in analytical studies [16-20].

CNT modified electrode can impart strong electrocatalytic activity to some important biomolecules such as cytochrome *c* [21, 22], NADH [23], hydrogen peroxide [24, 25] and catecholamines such as dopamine [26] and ascorbic acid. It leads to a strong interfacial accumulation of the substrate that can serve as a preconcentration step for highly sensitive adsorptive stripping measurements**.** Considering the importance of the above mentioned modified electrodes in the improvement of sensitivity, they are employed in the present

Till date, no publications concerning the electroanalytical determination of antihypertesive drugs in pharmaceutical formulations are available in the literatures. Therefore, the aim of the present investigation is to investigate the electrochemical behavior of antihypertesive drugs on MWCNTs modified glassy carbon electrode and to develop sensitive stripping voltammetric methods for the determination.

MATERIALS AND METHODS

Electrochemical Workstation (CH Instruments Model 760C) was employed mainly for carrying out electroanalytical studies. The three calcium channel blocker drugs of Lercanidipine, and Nifedipine were received from CIPLA Ltd, Mumbai, India and used as such.The stock solutions were made up in methanol/double distilled TKA-LAB purified water (80:20). For studies in aqueous methanol media, Britton Robinson buffers, 4.0, 7.0, 9.2, 0.1 mol.dm^{-3} KOH and 0.1 mol dm^{-3} H_2SO_4 were used as the medium for the analysis. Multiwalled CNTs produced by arc method was purchased from Sigma–Aldrich and sodium dodecyl sulphate (SDS) from Merck.

2.1. Procedure

Purging of nitrogen was done for analyte solution placed in the electrochemical cell of 15-ml capacity for 25 minutes under stirring and then voltammograms were recorded while blanketing nitrogen gas. To get reproducible results, great care was taken in the electrode pretreatment. The glassy carbon electrode was pretreated in two ways as described earlier [27].

2.2. Preparation of MWCNTs modified GCE

1mg MWCNT was dispersed in 1mL of 0.1M sodium dodecyl sulphate using an ultrasonicator to give black suspensions [28]. Cast films were prepared by placing 5μL of the MWCNT/surfactant suspensions on GCE and then evaporating it in an oven at 50 ◦C.

RESULTS AND DISCUSSION

3.1. Effect of pH

Britton–Robinson buffer/acid/alkaline solution was selected as the support electrolyte to find the optimal pH values for every analyte. The range of pH investigated was from 1.0 to 13.0. Values outside of this interval did not give either oxidation or reduction waves. Moreover, in some cases, signals were very close to the discharging current of the background, being very difficult the quantification. The pH affects both Ep and ip values. With respect to the first parameter, Ep values for the three pharmaceuticals decrease or increase in absolute value with pH, being more positive (Fig.1). Fig. 2 shows the dependence of ip with respect to pH for two drugs. From the curves, the optimal pH values for every one of them were deduced. This study was focused in order to find particular zones of potential for every compound that allowed the sequential determination of the two pharmaceuticals in a unique biological sample. From above discussion pH 13.0 was chosen as the best for further electrochemical studies.

3.2. Influence of modifier

Peak intensity (ip) and the peak potential (Ep) values using unmodified glassy carbon electrode and MWCNTs modified carbon electrode were studied. The modifier is expected to give to higher ip value and the longest distance from the discharging current of the background. The Ip and the Ep values are presented in figure 1 and 2. As it is observed, the MWCNTs modified electrode gives higher peak intensity values for all the pharmaceuticals. The modifier also influences the Ep values, although the shifts caused in the peaks of the analytes are not significantly relevant.

3.3. Cyclic voltammeric behavior of drugs

Cyclic voltammetric behaviour of the lercanidipine and nifedipine on MWCNTs modified glassy carbon electrode were carried out in pH 13.0. Figure 3 represent the cyclic voltammograms recorded for two drugs on modified glassy carbon electrode. They exhibited one oxidation peak with larger current and one reduction peak with lesser current. The anodic peak was taken for further discussion due its analytical characteristic because of larger peak

current. The peak potentials correlated well with log scan rate and resulted in straight lines. The fractional 'αn' value calculated from the slope confirmed irreversible electron transfer. The peak current showed increasing trend with sweep rate and straight lines with good correlation coefficients indicating adsorption. The plots, i_p vs. $\nu^{1/2}$ were curve lines (Fig.4) and log peak current vs log scan rate showed straight line (Fig.5) and its slope value is above 0.5.Thus it is further confirmed adsorption of the substrate on the pores and surface of the electrode and the overall reaction was adsorption controlled.

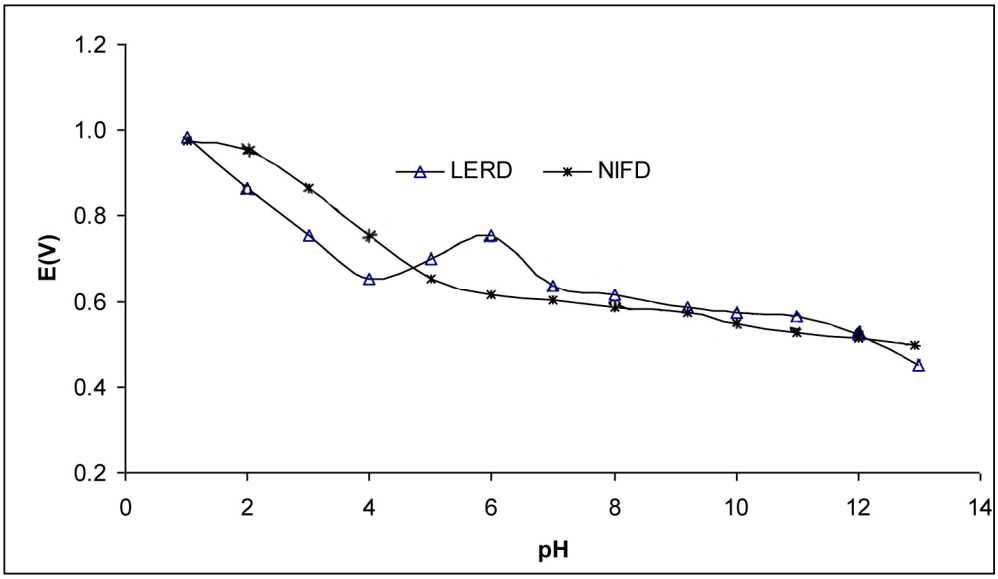


Fig.1. Plot of peak potential vs. pH

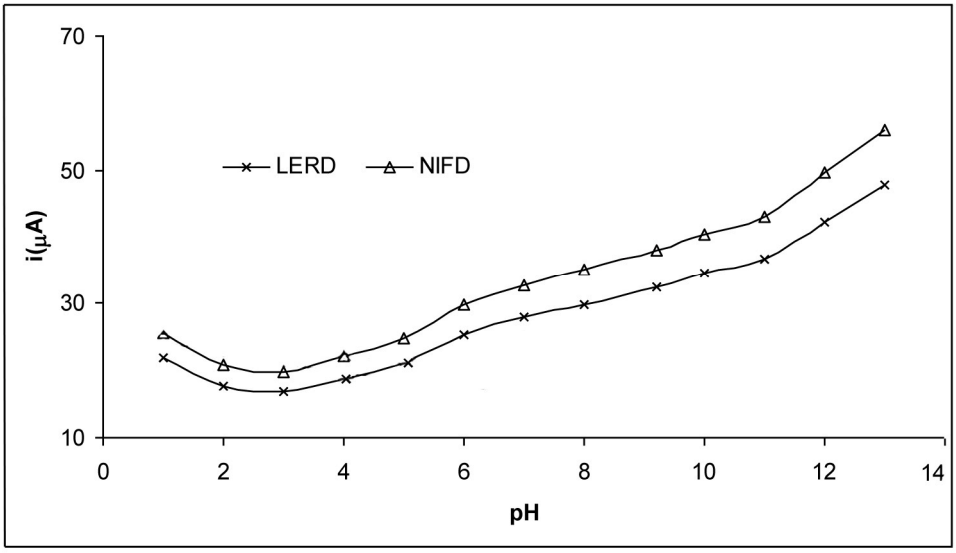


Fig.2. Plot of peak current vs. pH

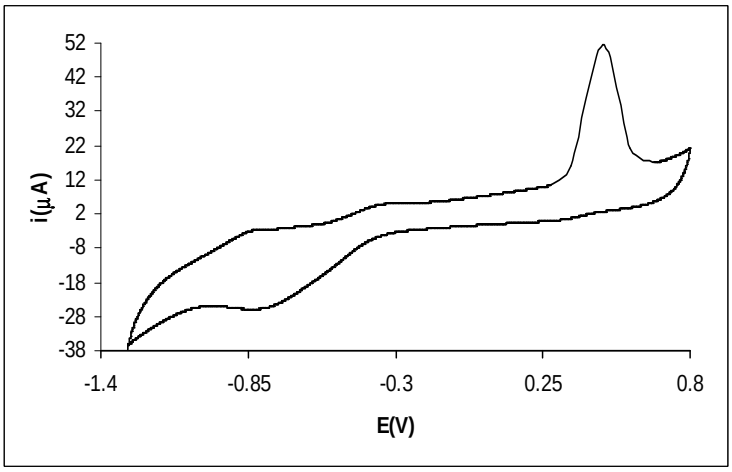


Fig.3a. Cyclic voltammogram of 305 μg/mL lercandipine on MWCNT/GCE at pH 13.0; scan rate 100 mV/s

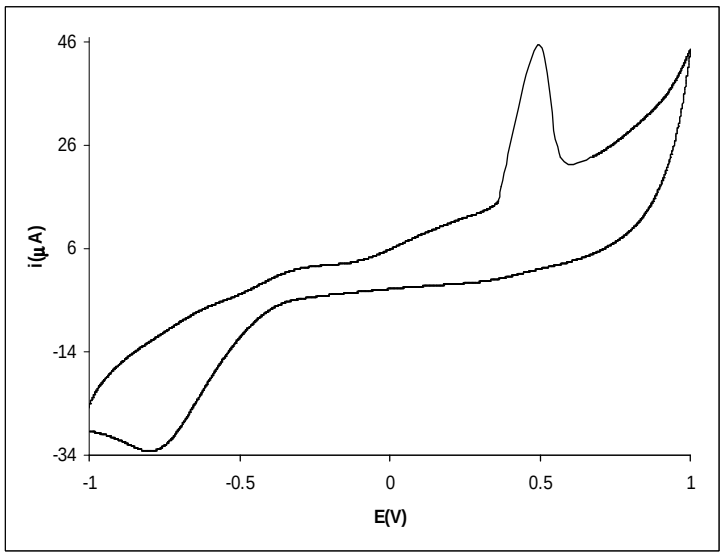


Fig.3b. Cyclic voltammogram of 175 μg/mL nifedipine on MWCNT/GCE at pH 13.0; scan rate 100 mV/s

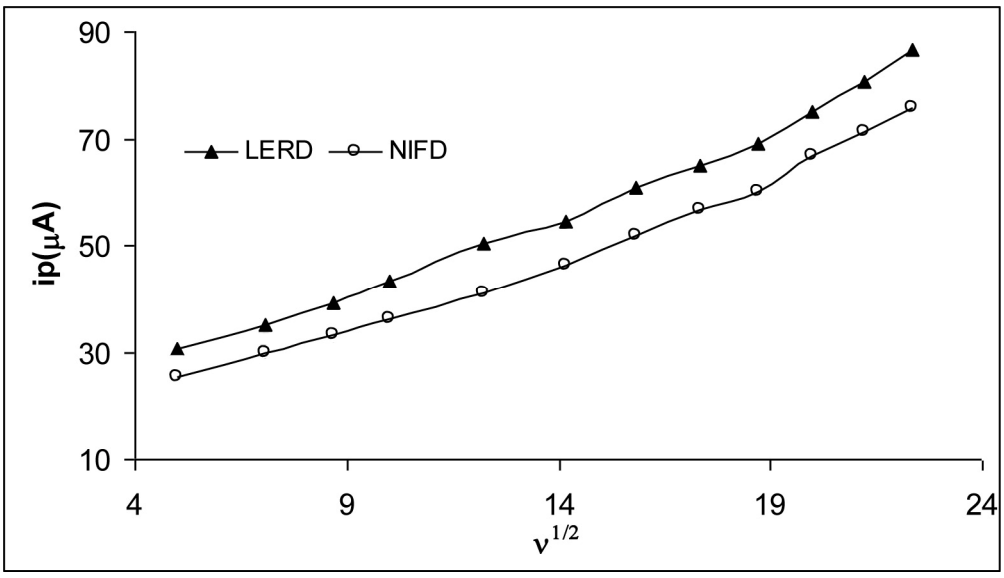


Fig.4. Plot of peak current vs. square root of scan rate

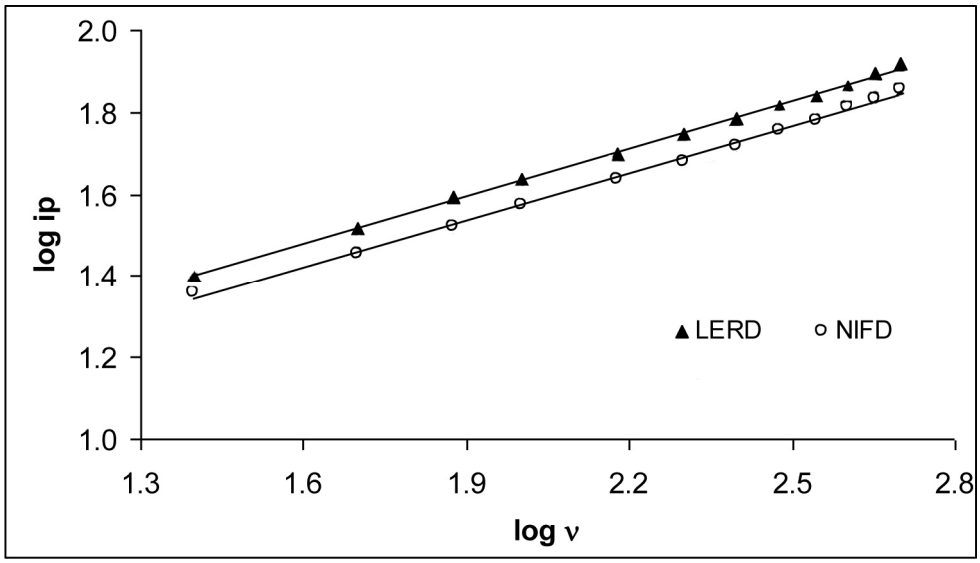


Fig.5. Plot of log peak current vs. log scan rate

3.4. Differential pulse stripping voltammetry (DPSV)

DPSV experiments were carried out to ascertain the best conditions for the adsorption process. Many preconcentration-stripping experiments were performed for different accumulation potentials (E_{acc}) and at an accumulation time (t_{acc}) of 10 seconds, to evaluate the electrostatic attraction/repulsion between electrode surface and the drugs. When accumulation potential changed from −0.1 to +0.5V, the maximum responses were obtained at 0.1V for the drugs. Maximum peak current was found for an accumulation potential in the positive region at 0.1V because of the electrostatic interaction between the positive nature of electrode at this potential and the electron rich substrate. After fixing the accumulation potential, the accumulation time was varied between 10 to 60 s. Maximum peak current was observed for LERD and NIFD at 10 s respectively. The decreased current above the maximum current signal condition might be due to saturation of the electrode surface and blocking of the products formed on the surface. The accumulation of the drugs on the modified electrode surface was ascertained by carrying out SEM analysis.

SEM was employed to study the surface morphology of the three accumulated drugs on MWCNTs coated glassy carbon electrode. The stem like structure of the coating confirmed the presence of MWCNTs on GCE. The average tube size of the material is 50 nm as reported earlier by us [27, 28]. The drug LERD adsorbed on MWCNTs electrode during accumulation and exhibited sponge with granular like structure (Fig 6a) and NIFD exhibited irregular broken like structure (Fig. 6b). Different surface morphology confirmed the accumulation of drugs on theMWCNTs/GCE

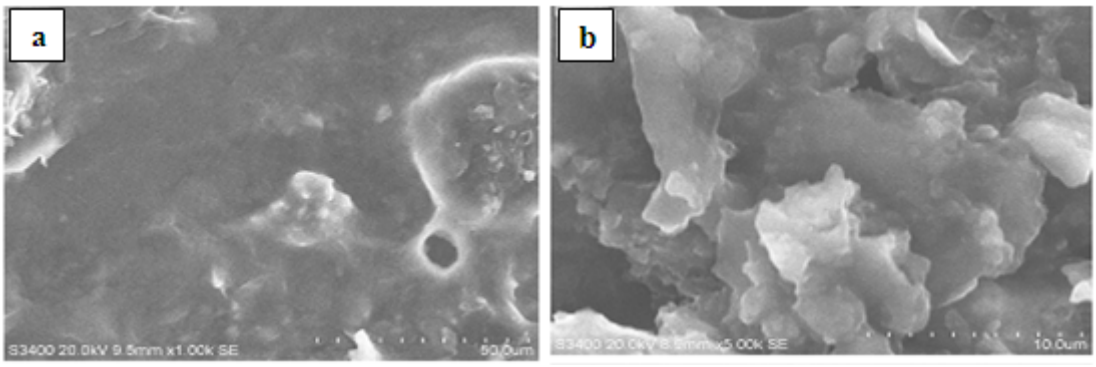


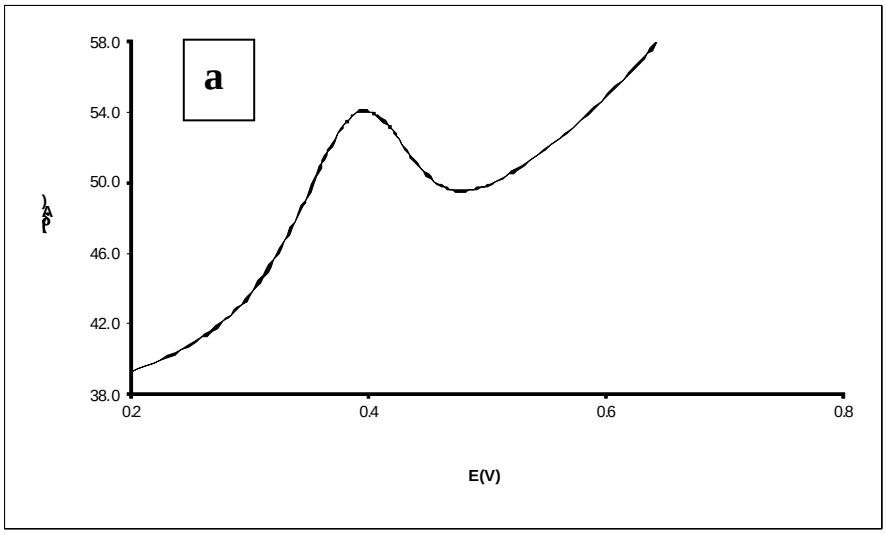
***Fig.6.* SEM photographs of (a) LERD and (b) NIFD on MWCNT modified GCE**

The initial scan potential, (E_{is}), was also an important parameter in controlling both peak potential and peak height in the stripping voltammogram. The initial potential was varied between –0.2 to 0.2 V and an initial scan potential at

-0.2V for LERD, and 0 .2V for NIFD led to higher peak current response. Pulse height was varied between 0.025 and 0.15 V. This variation had shown a decrease in peak current with increase in applied pulse height after 0.05V. Hence, pulse height of 0.05 V was chosen due to increased current response for all drugs. The effect of pulse period demonstrated that the stripping peak current increased up to 50 ms and then decreased with an increase in pulse width from 25 to 125 ms for the drugs. The peak current decreased with an increase in pulse width from 25 to 150 ms and a pulse width of 50 ms was selected. Thus, the maximum peak current conditions were arrived at and the results are presented in table 1. These conditions were used to study the effect of concentration.

Table 1.Optimum experimental conditions in DPSV

Variable	Range studied		Optimum value	
	LERD	NIFD	LERD	NIFD
pH	1.0-13.0	1.0-13.0	13.0	13.0
Accumulation potential (V)	-0.1 to 0.4	0.1 to 0.5	0.3	0.4
Accumulation time (Sec)	10-60	10-60	10	10
Initial scan potential (V)	-0.2 to 0.2	-0.2 to 0.2	-0.2	0.2
Pulse Height (PH) (mV)	25 to 150	25 to 150	75	50
Pulse width (PW) ms	25 to 150	25 to 150	50	50
Scan Increment (SI) mV	2 to 20	2 to 20	4	4
Stirring rate (rpm)	50 to 150	50 to 150	150	150
Rest period (Sec)	2 to 10	2 to 10	2	2



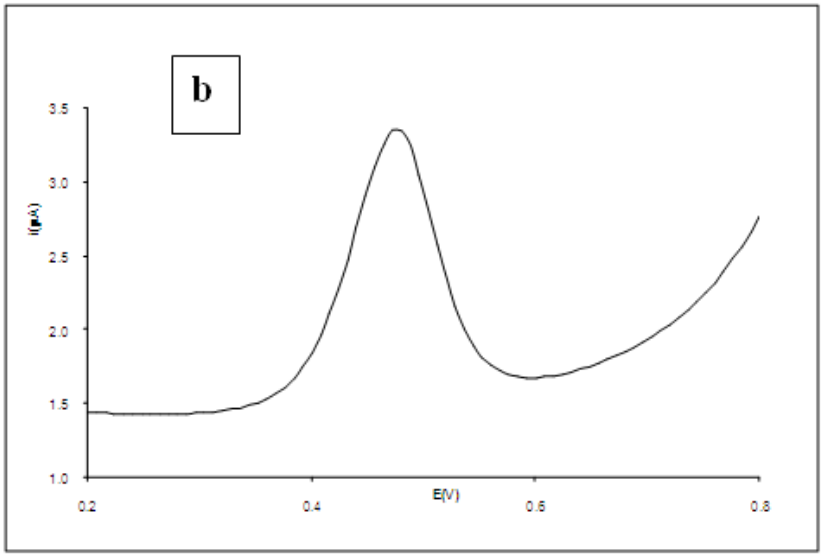


Fig.7. DPSV of (a) LERD and (b) NIFD under optimum conditions on MWCNT modified GCE

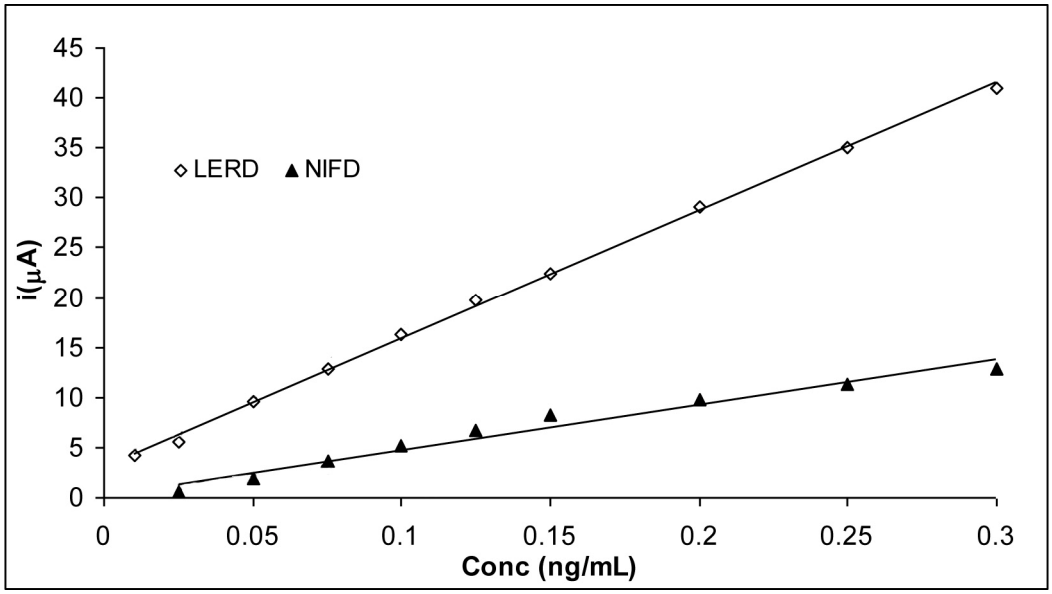


Fig.8. Calibration plot of peak current vs. concentration

3.5. Analytical Characteristics

Typical differential pulse stripping voltammogram for LERD, and NIFD obtained under the maximum peak current experimental conditions were presented in figure 7. As the concentration of the drugs increased, the stripping peak current increased. Calibration plots were made and presented in figure 8. The limits of concentration were 0.02 to 0.3μg/mL for LERD and 0.025 to 0.3μg/mL for NIFD. The LOD is 0.004μg/mL for LERD and 0.03μg/mL for NIFD. The precision of the method was ascertained by measuring the peak current of the drugs response in five standard samples. Ten replicates were analyzed and standard deviations were calculated. The relative standard deviation was 2.7% for a concentration 50 μg/mL of LERD, and 2.8% for 50 μg/mL of NIFD. The low value of standard deviation indicated good reproducibility and feasibility of this method for the determination of drugs.

3.6. Pharmaceutical sample analysis

In order to evaluate the applicability of the proposed method, commercial samples in combination or in pure form containing anyone of LERD, and NIFD were selected. The pharmaceutical samples were collected from medical shops at Karaikudi, Tamilnadu, India. Various tablets having LERD, and NIFD were examined for estimation of content of drugs. The tablets were dissolved in methanol and then the filtrate was further evaporated to get the drug in pure form. The residue was dissolved in known quantity of methanol and transferred into a 250 ml calibrated flask and made up to the mark. A 10 ml portion of this solution was transferred into a 50 ml calibrated flask and 0.1 mM NaOH containing 50% aqueous methanol was used to dilute the contents of the flask to the required volume. The standard addition method was used. 0.05 ml aliquot of the 0.1μg /mL standard stock solution was added to the solution prepared as described above. Differential pulse stripping voltammetric studies under the maximum current signal experimental conditions were carried out and the trace amount of drugs in the sample were determined. A relative standard deviation of 2.7% was obtained for 0.1μg/mL LERD for ten identical measurements. The relative standard deviation of 2.8 % was obtained for 0.1 μg/mL of NIFD for ten identical measurements. Thus the suitability of this method for the determination of LERD, and NIMD in real sample was verified. The results are presented in the table 2.

Table 2, Amount of drugs in tablets determined by DPSV in tablets

Brand name	Company name	Tablets in mg	Experimental value, mg	% RSD value
Lercanidipine(LERD)				
Lerez	Glenmark	10	9.65	2.7
Nifedipine(NIFD)				
Calcigard Retard	Torrent	20	19.69	2.4
Cardif Beta 10	Concept	10	9.75	2.7
Cardules Retard	Nicholas Piramal	20	19.42	2.2
Cardules Plus 10	Nicholas Piramal	10	9.59	2.8
Depicor SR	Merck	20	19.69	2.7

CONCLUSION

MWCNTs-modified GCE allowed the successful determination of LERD, and NIFD drugs with a detection limit of 0.004μg/mL for LERD and 0.03μg/mL for NIFD. The anodic peak current varies linearly under optimized conditions in the concentration range from 0.02 to 0.3μg/mL for LERD and 0.025 to 0.3μg/mL for NIFD. The results obtained are promising and demonstrate the utility of the developed method for the determination of drugs in pharmaceutical formulations. The specificity of the voltammetric method was also investigated in the presence of substances present in drugs. Thus, present investigation revealed that the proposed method is simple, specific, sensitive and effective for the determination of 1, 4-Dihydropyridines at MWCNTs-modified glassy carbon electrode in pharmaceutical formulations.

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