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Multiwall carbon nanotube based electrochemical sensor for nitrendipine, an antihypertensive drug

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Modified electrodes play a significant role in the development of electrochemical sensors. Nanomaterials are widely employed now-a-days for modification because of their electrocatalytic properties and enhanced surface area available for redox reactions. In the present study, multiwall carbon nanotube (MWCNT) modified electrode has been used as an electrochemical sensor for nitrendipine, an important antihypertensive drug. Cyclic voltammograms of nitrendipine exhibit a sharp anodic peak around 440 mV and one broad cathodic peak. Influence of sweep rate and concentration on the peak current and potentials have been investigated. Straight line with good correlation is obtained when the peak current was correlated with the sweep rate. The log peak current and log sweep rate plot yield a slope above 0.5 suggesting adsorption controlled reaction. Nitrendipine show enhanced peak current and decreased peak potential indicating good electrocatalytic activity towards the oxidation, leading to a marked improvement in sensitivity. This drug has been determined by differential pulse adsorptive stripping voltammetry. Systematic variation of pre-concentration and stripping parameters result in optimum values. Calibration plot in the linear concentration range 0.01 to 0.3 ng/mL is made and LOD is determined. This electrochemical sensor is successfully used for the determination of the drug in commercial samples.

Keywords : Nitrendipine, Cyclic voltammetry, Stripping voltammetry, Multiwall carbon nanotubes, Electrocehmical sensor

Various aspects of electrochemical radical ion generation and flowcell operation were discussed several decades ago, their relevance to cells using porous electrodes was similarly portrayed, and advanced concepts of analysis involving axial and radial dispersion have also been presented. As a further exploration, the purpose of the current paper is to demonstrate the usefulness of sequential batch/flow operational modes for the containment of unstable radicals, i.e., for the sustenance of the radicals at a pre-determined (mean) concentration level throughout the entire operation. The generation of the nitro-radical anion from nitrendipine (NITD) in certain endobiotic media serves as an example for quantitative illustration. The containment of unstable radical ions, the product of a rapid electrode reaction, is described by means of various flow regimes and electrode-potential forms have been reported[1]. Recently, the reduction mechanism of nitro aromatic compounds in aqueous medium has been deeply examined[7]. The results were presented and analyzed in detail in that the article constitute was an excellent illustration of the complexity of the reduction mechanism of nitroaromatics in aqueous medium, essentially because of the two factors, adsorption and protonations. The electrochemistry of 4-(nitrophenyl) substituted 1,4-dihydropyridine (1,4-DHP) have been extensively studied in the last years[2].

Generally, MWCNT based electrodes enhance the detection sensitivity and improve reversibility as it can promote electron transfer[3]. Perusal of literature reveals only few publications[4,5] concerning the electroanalytical determination of antihypertensive drugs in pharmaceutical formulations. Because of the importance of MWCNT modified electrodes for drug determinations, electrochemical study of antihypertensive drug using MWCNT modified glassy carbon electrode was carried out and a sensitive stripping voltammetric method for the determination was developed.

Experimental Section

Electrochemical Workstation (CH Instruments Model 760C) was employed mainly for carrying out electroanalytical studies. Nitrendipine (NITD) were received from CIPLA Ltd, Mumbai, India and used as such.

The stock solutions were made up in aqueous methanol (80:20). The double distilled TKA-LAB purified water was used for all the experiments. Britton Robinson buffers, og *p*H 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 and the *p*H was measured using Cyberscan *p*H meter. MWCNT

produced by arc method was purchased from Sigma–Aldrich and sodium dodecyl sulphate (SDS) from Merck.

Procedure

Purging of nitrogen was done for analyte solution placed in the electrochemical cell of 15-mL capacity for 25 min 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[6].

Preparation of MWCNTs Modified GCE

1mg MWCNT was dispersed in 1mL of 0.1M sodium dodecyl sulphate using an ultrasonicator to give black suspension[7]. The MWCNT/surfactant suspension was casted on GCE by placing 5μL and then evaporated in an oven at 50°C to get a uniform film.

Result and Discussion

Effect of *p*H

The effect of *p*H was studied in detail by choosing different *p*H conditions viz. 1.0 to 13.0. Figures 1&2 shows the variation of peak potential and current respectively with *p*H. The drug exhibited decreasing trend in peak potential with increase in *p*H. At basic *p*H, only one anodic peak and one broad cathodic peak were observed. The peak current showed increasing trend with increasing *p*H up to basic *p*H (Fig. 2). The peak current exhibited maximum value at *p*H 13.0. From analytical point of view, *p*H 13.0 was chosen for the development of electroanalytical determination procedure for the drug on MWCNT modified glassy carbon electrode owing to maximum peak current responses. The increase in peak current may be due to the increase in the electroactive surface area due to modification of the glassy carbon surface with MWCNT and higher electrocatalytic activity at *p*H 13.0

Cyclic voltammetric studies of NITD

Cyclic voltammetric studies of NITD at pH 13.0 were carried out on MWCNT modified GCE. The sweep rate was varied from 25 to 500 mVs^{-1}. In the entire scan rate, only one anodic peak was observed around 440 mV in cyclic voltammograms with high peak current values and is considered for detailed discussions. A representative cyclic voltammogram is presented in Fig. 3. The oxidation of NITD is taking place at 440 mV potential but the peak exhibits high peak current.

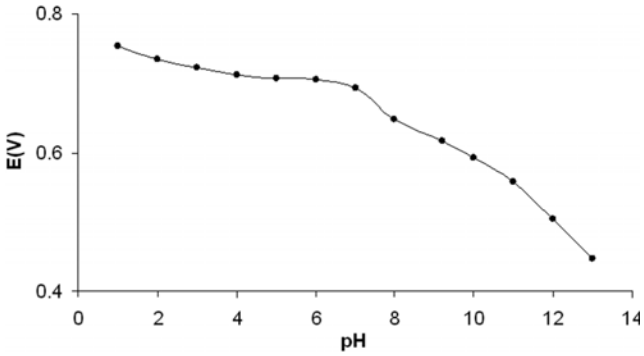

Fig. 1 — Plot of potential vs. *p*H

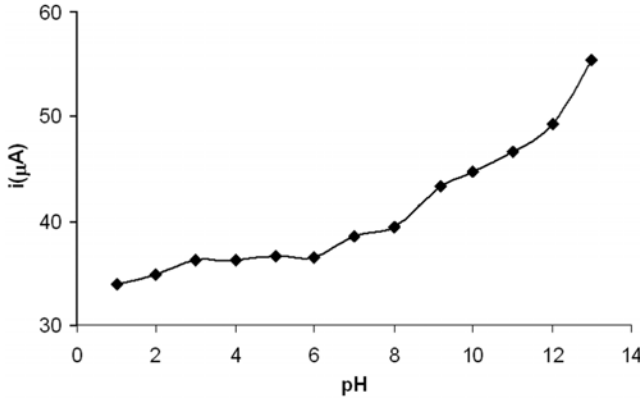

Fig. 2 — Plot of peak current vs. *p*H

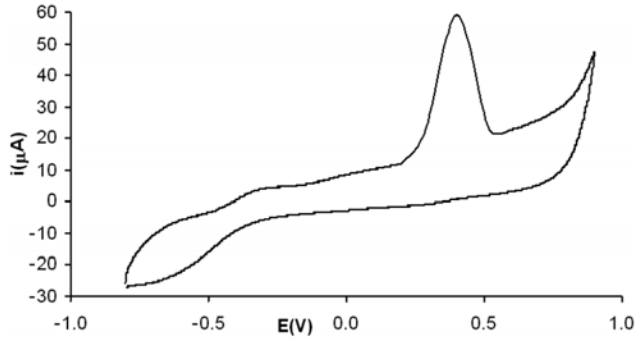

Fig. 3 — Cyclic voltammogram of NITD on MWCNT/GCE at *p*H 13.0

There is no satisfying reversibility in the reverse scan for the anodic peak. The E_p vs. log ν plot leads to a straight line with good correlation. *αn* value was calculated from the slope. It was found to be fraction (0.512). Hence the electron transfer is said to be irreversible. The peak current was correlated with scan rate and a slight curved line obtained. The plot i_p vs. $\nu^{1/2}$ gave a straight line with very good correlation coefficient (r^2 = 0.9972). The log i_p vs. log ν plot resulted in a straight line with slope value of 0.5109. Hence the reaction can be concluded as adsorption controlled. Increase in the concentration of NITD

showed increased peak current and gradual increase in peak potential. The anodic peak showed a shift to anodic side.

Differential pulse stripping voltammetry of drug

CV studies revealed that adsorption of NITD would result in accumulation of more molecules on MWCNT/GCE. Hence DPSV experiments were carried out using MWCNT/GCE to develop more sensitive analytical procedure for the determination of NITD. Many pre-concentration and stripping experiments were performed to ascertain the optimum experimental parameters. In the accumulation step, the effect of accumulation potentials (E_{acc}) and accumulation time (t_{acc}) was studied to evaluate the electrostatic attraction/repulsion between electrode surface and the drugs. When accumulation potential was changed from −100 to 500 mV at an accumulation time, 15 s, the maximum peak current responses were obtained at 300 mV for all the three drugs. This suggests an electrostatic attraction between the slightly positive nature of electrode at 300 mV and the electron rich substrates. After fixing the accumulation potential as 300 mV, the accumulation time was varied between 10 to 60 s. Maximum peak current was observed of NITD at 20 s. 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 drug on the modified electrode surface was ascertained by carrying out SEM analysis.

SEM was employed to study the surface morphology of the accumulated drugs on MWCNT/GCE. As reported by us earlier[7, 8], MWCNT on GCE had stem like structure and the average tube size of the material was 50 nm. The drug NITD adsorbed on MWCNT/GCE during accumulation and exhibited bigger void foam like structure (Fig. 4). Different surface morphology confirmed the accumulation of drugs on the MWCNT/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 – 100 and 300 V and an initial scan potential of 200 mV of NITD led to higher peak current response. Pulse height was varied between 25 and 125 mV. This variation had shown a decrease in peak current with increase in applied pulse height after 50 mV. Hence, pulse height of 50 mV was chosen due to increased current response of drug. The effect of pulse period demonstrated that the stripping peak current increased up to 50 ms and then decreased with an increase in pulse period from 75 to 125 ms for all the three drugs. The peak current decreased with an increase in pulse width from 25 to 100 ms and a pulse width of 50 ms was selected. The maximum peak current conditions were arrived and the results are presented in Table 1. These conditions were used to study the effect of concentration.

Analytical characteristics

Typical differential pulse stripping voltammogram of NITD obtained under the maximum peak current experimental conditions were presented in Fig. 5. As the concentration of the drug was increased, the stripping peak current increased. Calibration plots were made and presented in Fig. 6. The analytical ranges of concentration were 0.01 to 0.3 μg/mL of NITD. The LOD of NITD is 0.005 μg/mL. The precision of the method was ascertained by measuring

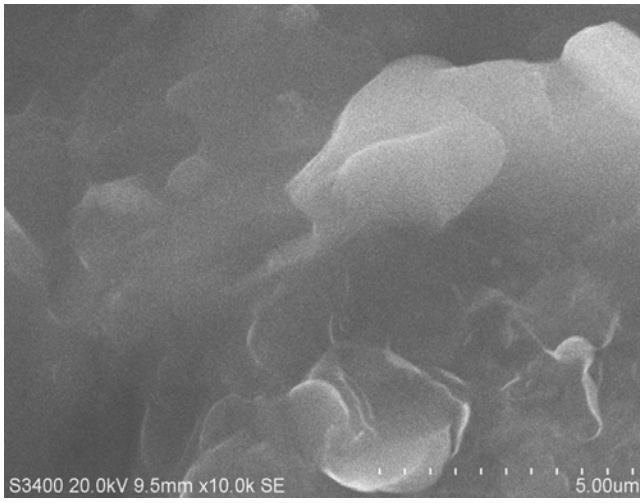

Fig. 4 — SEM photographs of NITD on MWCNTs/GCE

Table 1 — Optimum experimental conditions in DPSV

Variable	Range studied	Optimum value
*p*H	1.0-13.0	13.0
Accumulation potential (V)	-0.1 to 0.4	0.3
Accumulation time (S)	10-60	20
Initial scan potential (V)	-0.4 to 0.2	0.2
Pulse Height (PH) (mV)	25 to 150	50
Pulse width (PW) mS	25 to 150	50
Pulse period (PP) mS	25 to 150	50
Scan Increment (SI) mV	2 to 20	4
Stirring rate (rpm)	50 to 250	150
Rest period (S)	2 to 10	2

the peak current of the drug in five standard samples. Ten replicates were analyzed and standard deviations were calculated. The relative standard deviation was 2.5% of NITD. The low value of standard deviation indicated good reproducibility and feasibility of this method for the determination of drug.

Pharmaceutical sample analysis

In order to evaluate the applicability of the proposed method, ten commercial samples in combination or in pure form containing anyone of NITD was selected. The pharmaceutical samples were collected from medical shops at Karaikudi, Tamilnadu, India. Various tablets having NITD was examined for the estimation of drug. 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 to a 250 mL calibrated flask and made up to the mark. A 10 mL portion of this solution was transferred to 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 0.1 μg/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 drug in the sample were determined. A relative standard deviation of 2.5% was obtained for 0.1 μg/mL NITD for ten identical measurements. Thus the suitability of this method for the determination of NITD 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
Nitrepin	USV	20	19.95	2.1
Cardif	Concept	20	19.90	2.4

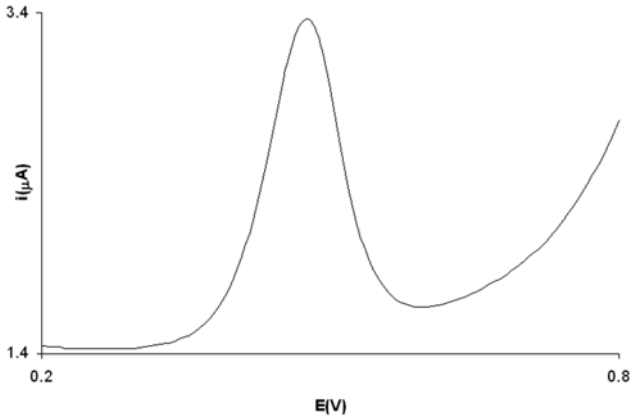

Fig. 5 — DPSV of NITD under optimum conditions

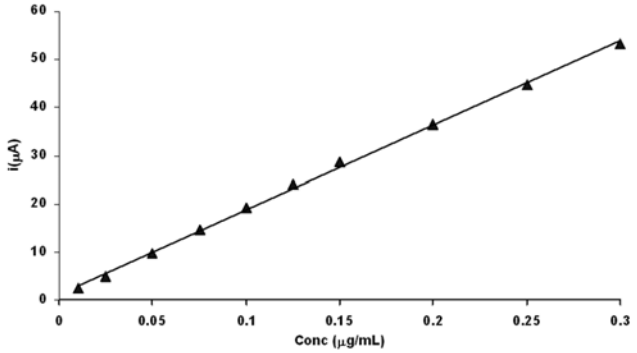

Fig. 6 — Calibration plot of peak current vs. concentration

Conclusion

The electrochemical behavior of nitrendipine was examined for the first time with this study. The voltammetric oxidation steps of nitrendipine in different buffer solutions of *p*H 1.0- 13.0 have been elucided with MWCNT/GC electrode. The detailed electrooxidation outcome of nitrendipine at MWCNT based electrodes used for analytical purposes, particularly as a sensor. Fully validated, highly selective and sensitive, simple and precise voltammetric procedures were described for determination of nitrendipine in bulk form and pharmaceutical dosage samples without the necessity of sample pre-treatment or time-consuming extraction and evaporation steps prior to the analysis.

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