

# Electrochemical Stripping Studies of Amlodipine Using Mwcnt Modified Glassy Carbon Electrode

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## Abstract

The voltammetric behaviour of amlodipine was studied on multiwall carbon nanotubes (MWCNT) modified glassy carbon electrode. The oxidation of amlodipine is irreversible and exhibits a diffusion controlled process which is pH dependent. The oxidation mechanism was proposed in this work. The dependence of the current on pH, the concentration and nature of buffer, and scan rate were investigated to optimize the experimental conditions for the determination of amlodipine. Calibration plots were drawn between stripping peak current and concentration. They are linear within the range from 0.01 to 0.3µg/mL. The lower limit of detection (LOD) was found to be very low (0.001µg/mL) on MWCNT. The developed MWCNT modified glassy carbon electrode system was applied to successfully determine amlodipine in commercial pharmaceutical products.

**Key Words:** Voltammetric, Multiwall Carbon Nanotubes, Amlodipine, Stripping.

## 1. INTRODUCTION

Considering that amlodipine (AMLD) is a novel drug, few analytical methods for its determination have been described. Among them, a capillary electrophoresis method has been devoted to assay both the enantiomer and diastereomers purity and recently the enantioseparation of dihydropyridine derivatives by means of neutral and negatively charged  $\beta$ -cyclodextrin derivatives using capillary electrophoresis has been described [1]. HPLC with electrochemical detection has been applied to the determination of several of the studied compounds and other 1,4-dihydropyridines in biological fluids [2], but it has not been used for the analysis of these drugs in pharmaceutical formulations. [3]

Dihydropyridine calcium antagonists as a class are powerful antihypertensive drugs and offer a tool to achieve goal blood pressure levels when given singly or in combination with other classes of drugs. However, the utility of these compounds has been questioned on the grounds of their adverse hemodynamic, renal, and sympathetic nervous system effects. From a pharmacologic dimension, amlodipine appears to have a long duration of action despite its short plasma half-life, indicating that the drug accumulates in the vascular tissue, thereby producing significant and sustained vasorelaxation [4]. In this work, amlodipine is coated on MWCNT modified glassy carbon electrode for differential pulse stripping voltammetrically.

## 2. EXPERIMENTAL

Electrochemical Workstation (CH Instruments Model 760C) was employed mainly for carrying out electro analytical studies. The calcium channel blocker drugs of amlodipine(AMLD)as 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, 0.1mol.dm<sup>-3</sup>

$^3\text{KOH}$  and  $0.1 \text{ mol dm}^{-3} \text{ H}_2\text{SO}_4$  were used as the medium for the analysis. MWCNT's 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 analytic 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 [5].

### 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 [6]. Cast films were prepared by placing  $5\mu\text{L}$  of the MWCNT/surfactant suspensions on GCE and then evaporating it in an oven at  $50^\circ\text{C}$ .

## 3. RESULTS AND DISCUSSION

### 3.1 EFFECT OF pH

The effect of pH was studied in detail by choosing three different pH conditions viz. acid, neutral and basic. Fig. 1 and 2 shows the variation of peak potential and current respectively with pH. Usually in acidic medium, the proton availability is excess and hence protonations become fast. The drug exhibited decreasing trend in peak potential with increase in pH. At basic pH, only one anodic peak and one broad cathodic peak were observed. The peak current shows increasing trend with increasing acidic pH to basic pH (Fig. 2). The drug of amlodipine exhibited maximum peak current value at pH 13.0. From analytical point of view, pH 13.0 was chosen for the development of electro analytical determination procedure on MWCNT modified glassy carbon electrode owing to the maximum peak current responses. The increase in peak current may be due to the increase in the electro active surface area attained by the modification of the glassy carbon surface with MWCNT and higher electro catalytic activity at pH 13.0.

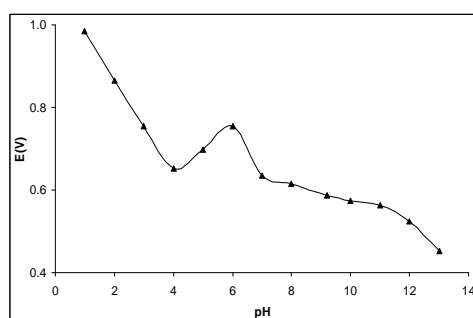


Fig.1. Plot of peak potential vs. pH

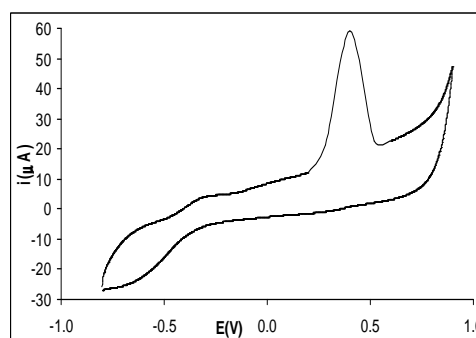


Fig.2. Plot of peak current vs. pH

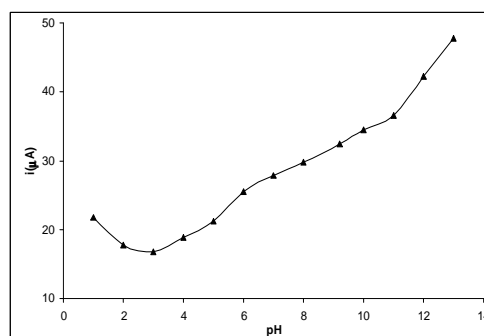


Fig.3. Cyclic voltammogram of  $305 \mu\text{g/mL}$  amlodipine on MWCNT/GCE at pH 13.0; scan rate  $100 \text{ mV/s}$

Cyclic voltammograms of AMLD at an optimum pH 13.0 showed one anodic peak around potentials 590 mV and one broad cathodic peak around -680 mV (Fig.3). The anodic peak with higher current was considered for correlation studies. It increased with increase in scan rate. Two plots,  $i_p$  versus  $v$  and  $i_p$  versus  $v^{1/2}$  ( $R^2 = 0.999$ ) were plotted. Plot of  $\log i_p$  vs  $\log v$  results in a straight line with slope value is 0.5336. These factors indicate that the oxidation of AMLD was adsorption controlled.

The cathodic peak and anodic peak did not satisfy the reversibility condition. Plot of  $E_p$  vs.  $\log v$  resulted in a straight line and the transfer coefficient ' $\alpha$ ' was calculated to be 0.6233. Hence the oxidation of AMLD is considered to follow irreversible de-electro nation. The effect of concentration was studied as before. The peak potential and peak current increased with increase in concentration.

The diffusion coefficient,  $D$  was determined for  $1.3 \times 10^{-7} \text{ M/cm}^3$  concentration of AMLD at pH 13.0 by chronocoulometric experiment. The plot of  $Q$  versus  $t^{1/2}$  obtained at pH 13.0 is presented in figure 4. Diffusion coefficient  $D$  was calculated from the value of forward slope obtained and was found to be  $1.7 \times 10^{-5} \text{ cm}^2/\text{s}$  at pH 13.0. Rounded coulometric ' $n$ ' value was taken and used for the calculation.

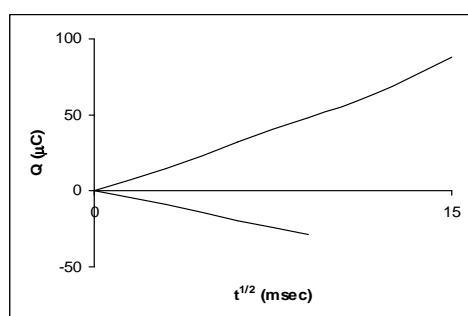


Fig.4. Plot of charge vs. square root of time

At pH 13.0,  $4.5 \times 10^{-7} \text{ M/dm}^3$  concentration of AMLD was chosen for controlled potential coulometric study. The potential was maintained at 458 mV for exhaustive electrolysis. From the charge versus time plot presented in figure 5,  $Q$  was obtained and ' $n$ ', the coulometric number of electrons transferred was calculated using the equation  $Q = nFN$ . At pH 13.0, ' $n$ ' is found to be around 2.

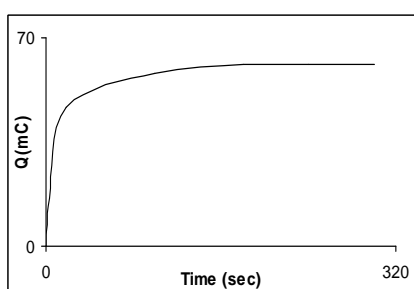
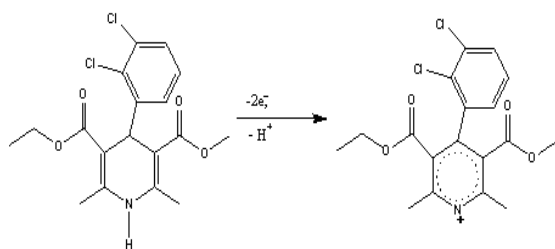


Fig.5. Plot of charge vs. time

From the above studies and number of electrons transferred, the dye AMLD molecule is said to undergo an oxidation involving two electrons. The modification of GCE with MWCNT resulted in maximum peak current and hence it is opted for electro analytical determination of AMLD.

### 3.2 REACTION MECHANISM

The proposed mechanism may be assigned to the amino group undergoing a redox reaction, at pH 13 as given below.



### 3.3 DIFFERENTIAL PULSE STRIPPING VOLTAMMETRY (DPSV) OF AMLODIPINE

Cyclic voltammetry studies revealed that amlodipine would result in accumulation of more molecules on MWCNTs/GCE. Hence DPSV experiments were carried out using MWCNTs/GCE to develop more sensitive analytical procedure for the determination of AMLD. 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, 15s, the maximum peak current responses were obtained at  $100$  mV. This suggests an electrostatic attraction between the slightly positive electrode potential at  $100$  mV and the electron rich substrates. After fixing the accumulation potential at  $100$  mV, the accumulation time was varied between  $10$  to  $60$  s. Maximum peak current was observed at  $10$  s. The decreased current above the maximum current signal condition might be due to the 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 accumulated drug on MWCNT/GCE is mentioned in the experimental part [5, 6], MWCNT on GCE had exhibited broken pitch and sponge like structure of the material was  $50$  nm. The drug adsorbed on MWCNT/GCE during accumulation and exhibited a structure similar to granular sponge (Fig. 6) Different surface morphology confirmed the accumulation of drugs on the MWCNT/GCE.

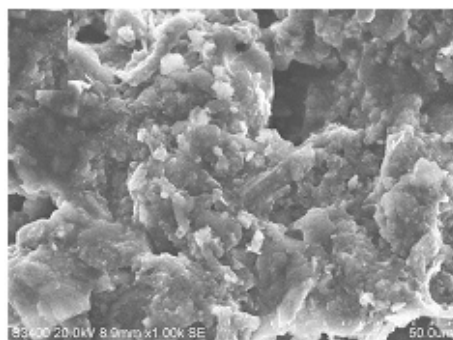


Fig.6. SEM photograph of amlodipine on MWCNT/GCE

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 varied between  $-400$  to

300 mV and an initial scan potential of 200 mV led to higher peak current response. Pulse height varied between 5 and 25 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. It was demonstrated that the stripping peak current increased up to 50 ms and then decreased with an increase in pulse width from 75 to 125 ms. The peak current decreased with an increase in pulse width from 75 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 table1. These conditions were used to study the effect of concentration.

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

Table 1. Optimum experimental conditions in DPSV on MWCNT/GCE

### 3.4 ANALYTICAL CHARACTERISTICS

Typical differential pulse stripping voltammogram of AMLD 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 plotted and presented in figure 8. The analytical range of concentration was 0.01 to 0.3  $\mu\text{g/mL}$ . The LOD was 0.001  $\mu\text{g/mL}$ . The precision of the method was ascertained by measuring the peak current of the drug in six standard samples. Six replicates were analyzed and standard deviations were calculated. The relative standard deviation was 2.8% for a concentration 50  $\mu\text{g/mL}$  of AMLD. The low value of standard deviation indicated good reproducibility and feasibility of this method for the determination of presence of drug in biological fluids.

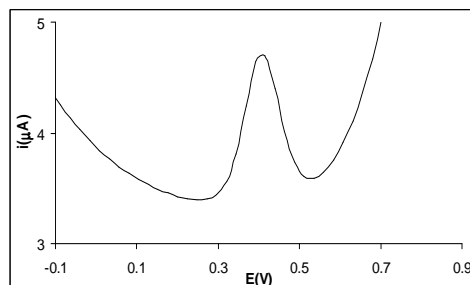


Fig.7. DPSV behavior of AMLD at optimum experimental conditions

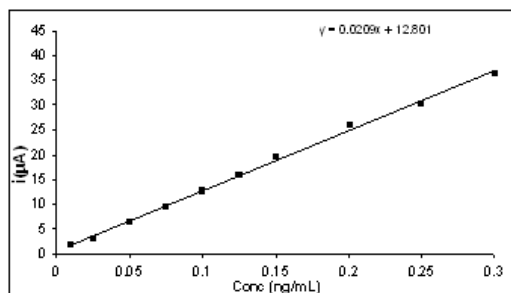


Fig.8. Calibration plot of peak current vs. concentration

### 3.5 PHARMACEUTICAL SAMPLE ANALYSIS

In order to evaluate the applicability of the proposed method, commercial samples in combination with AMLD were selected. The pharmaceutical samples were collected from medical shops at Karaikudi, Tamilnadu, India. Various tablets having AMLD were examined for the estimation 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 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 were carried out and the trace amount of drugs in the sample were determined. A relative standard deviation of 2.5% was obtained for 0.1 μg/mL AMLD for ten identical measurements. Thus the suitability of this method for the determination of AMLD in real sample was verified.

### 4. CONCLUSION

The biological sample of AMLD is a special type of compound, whose particular biological functions (pharmacological or toxicological) are possibly related to their redox properties. In aqueous methanol media, depending on the pH, the tendency of the compound is to get reduced via 2-electrons generating an electrochemical signal. Electrochemical approaches permit to obtain high current and low reduction potentials at pH 13.0. This permits the development of suitable electro analytical methods with respect to the compounds of biological significance.

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