CHAPTER - VII
SUMMARY OF THE INVESTIGATION

Calcium channel blockers are a class of drugs and natural substances that disrupt the conduction of calcium channels. It has effects on many excitable cells of the body, such as cardiac muscle, i.e. heart, smooth muscles of blood vessels, or neurons. Drugs used to target neurons are used as antiepileptics. The main clinical usage of calcium channel blockers is to decrease blood pressure. It is for this action that they are used in individuals with hypertension. Most calcium channel blockers decrease the force of contraction of the myocardium (muscle of the heart). This is known as the negative inotropic effect of calcium channel blockers. It is because of the negative inotropic effects of most calcium channel blockers that they are avoided (or used with caution) in individuals with cardiomyopathy. Many calcium channel blockers also slow down the conduction of electrical activity within the heart, by blocking the calcium channel during the plateau phase of the action potential of the heart. This results in a negative chronotropic effect resulting in a lowering of the heart rate and the potential for heart block. Electroanalytical chemistry plays an important role in the detection of traces of drugs and their destruction. This investigation throws more light on the electrochemical studies of drugs.

CHAPTER I
Introduction

This introductory chapter discusses the significance of electrochemical methods such as cyclic voltammetry, differential pulse voltammetry, chronocoulometry, controlled potential coulometry and stripping voltammetry in the elucidation of reaction mechanisms and analytical determinations in detail. The basic principles of cyclic voltammetry, chronocoulometry, controlled potential coulometry and stripping voltammetry are also
outlined. It also describes the role of stripping voltammetry in pharmaceutical analysis and the utility of solid sensors in the field of electrochemistry.

CHAPTE
R II
State of Art and Scope of the Investigation

This chapter discusses the reason for the selection of the six drugs namely, Amlodipine (AMLD), Felodipine (FELD), Lercanidipine (LERD), Nifedipine (NIFD), Nimodipine (NIMD) and Nitrendipine (NITD) and their general properties. The present status and earlier work carried out on the six drugs are also discussed here. The necessity for the present investigation on electroanalysis of drugs and the scope of the present investigation are described elaborately.

CHAPTE
R III
Experimental Details

Third chapter describes the instrumental aspects, methodologies and procedures employed during this investigation. This includes the description of CH Instrumentats Electrochemical Workstation Model 760C and Hitachi S3000 H SEM, cell setup, electrodes, pretreatment of electrodes, the chemicals employed, preparation of electrolyte and experimental methods for all electroanalytical studies. The procedures for various electrochemical techniques are also narrated in this chapter.

CHAPTE
R IV
ELECTROCHEMICAL STUDIES OF DRUGS ON GCE

Amlodipine (AMLD)

This chapter discussed the results obtained from the electrochemical studies of amlodipine in aqueous ethanol medium using glassy carbon electrode. Cyclic voltammetric studies were carried out at different pH ranging from 1.0 to 13.0. Detailed studies were
carried out at five-selected pH namely, 1.0, 4.0, 7.0, 9.2 and 13.0. Effect of sweep rate and concentration were studied in detail at these five pH conditions. Straight lines with good correlation were observed when the peak current was correlated with the sweep rate. Non-linear was observed between the peak current and square root of sweep rate. The log peak current and log sweep rate plot yielded a slope above 0.5. These factors suggested adsorption controlled reaction. From the slope of the plot peak potential, $E_p$ vs. log of sweep rate, the transfer coefficient was calculated. The absence of peak in the reverse scan and fractional transfer coefficient, the irreversibility of the electron transfer was understood. Controlled potential coulometry and the diffusion coefficient ‘D’ was experimentally found out from chronocoulometric studies determined number of electrons transferred in the oxidation process.

The following salient points are obtained from the electrochemical studies:

(1) pH 13.0 was selected as the best pH for the electrochemical studies of amlodipine.

(2) One main oxidation peak was observed in the cyclic voltammogram of amlodipine. This electron transfer here was found to irreversible and the reaction was adsorption controlled.

(3) The total number of electrons involved in the main oxidation process was two in all five pHs.

(4) On the basis of the results, a possible mechanism for the oxidation of amlodipine was proposed.

Felodipine (FELD)

In the electrochemical studies of felodipine, one main anodic peak was observed as in the previous compound. The effect of pH was studied by varying the pH between 1.0 and 13.0. Detailed study was carried out at selected pH only. Effect of sweep rate and
concentration were understood by correlating the peak current with sweep rate, square root of sweep rate and concentration. The plots log peak current vs. log sweep rate and peak potential vs. log sweep rate were also made. $E_p$ and $i_p$ values were correlated with pH value. Higher peak current and peak potentials were found at acidic pH. Chronocoulometric and controlled potential coulometric results were also discussed. All these studies revealed an irreversible electron transfer and the overall process was oxidation controlled. At pH 13.0, the number of electrons involved was two. The possible mechanistic scheme was given.

**Lercanidipine (LERD)**

In the voltammetric studies of lercanidipine, cyclic voltammograms of drug on glassy carbon electrode in acid, neutral and alkaline media at different sweep rates from 25 to 500 mV/s were recorded. At all concentrations and sweep rates studied, here also showed one anodic peak. Effect of pH was studied between 1.0 and 13.0. Effect of sweep rate and concentration were studied as in the previous studies. All the correlations were made. The results indicated the irreversible oxidation of drug and the reaction was controlled by adsorption. The adsorption coefficients were calculated from chronocoulometric results. The number of electrons transferred was determined from the controlled potential coulometric studies.

**Nifedipine (NIFD)**

Voltammetric studies of nifedipine using glassy carbon as working electrode were carried out by recording cyclic voltammograms in various aqueous ethanol pH media. It showed one oxidation peak in the potentials 630, 1170 and 1500 mV. In the reverse scan, one reduction peak at the peak potential was also observed. The sweep rate and concentrations were varied in each pH. The number of electrons transferred was calculated using controlled potential coulometry and bulk electrolysis was used to ascertain the product. Chronocoulometry was
employed to determine the diffusion coefficients. On the basis of the results, it was concluded that the electron transfer was irreversible and the overall process was said to be adsorption-controlled. The coulometric ‘n’ value was determined and it was found to be 2 at all pHs. A probable mechanism was proposed.

- **Nimodipine (NIMD)**

  Similar CV studies were carried out for NIMD at an optimum pH of 13.0 and only one anodic peak was observed. Plots of peak current versus scan rate resulted in straight line whereas the same with square root of scan rate resulted in a slight curved line. The slope value from the plot of log peak current vs. log scan rate was above 0.5. These factors suggest adsorption controlled anodic reaction. The absence of reversible counter part and the fractional transfer coefficient value conclude the irreversible nature of oxidation. The chronocoulometry and controlled potential coulometry indicate the number of electrons transferred to be two and hence the same mechanism discussed with GCE holds good here also.

- **Nitrendipine (NITD)**

  Electrochemical behaviour of NITD was observed at an optimum pH of 13.0. The cyclic voltammogram showed one anodic peak of which the anodic peak with high current response was considered for further analytical studies. The correlation studies represent the over all reaction to be irreversible and adsorption controlled. Peak current showed an increasing trend with increase in concentration. Chronocoulometric and controlled potential coulometric experiments were carried out and the reactions proceed with the same mechanism proposed for the bare glassy carbon electrode. Hence, it may be considered that the oxidation drug followed an irreversible adsorption controlled mechanism.
CHAPTER V
Electrochemical Studies of Drugs on Modified Electrodes

❖ At NaMM/GCE

This part presents the voltammetric studies of the six drugs using sodium montmorillonite clay modified glassy carbon electrode (NaMM/GCE) in aqueous ethanol medium. NaMM clay was coated on glassy carbon electrode dried and used for the studies. The electrochemical behaviour of the drugs on this modified electrode surface was studied using cyclic voltammetry.

Cyclic voltammograms were performed at pH 13.0 for all drugs. This medium was selected on the basis of the results obtained from cyclic voltammetric studies on NaMM/GCE. Various cyclic voltammograms of drugs were run at various sweep rates from 25 to 500 mV/s. As in the bare electrode studies, one oxidation and one reduction peaks were seen for all drugs. As evident from the voltammograms there was no satisfying irreversibility of reduction peaks in the reverse scan. From the correlation results, it was understood that the reaction was diffusion-controlled and the electron transfer was irreversible. Compared to the cyclic voltammetric studies at bare glassy carbon electrode, the potentials of the peaks were shifted to lower side. The reaction nature is diffusion controlled one. The oxidation of the substrate was facilitated because of the accumulation of the substrates in the pores of the NaMM clay. But the peak current was found to be slightly increased in all cases. Chronocoulometry, controlled potential coulometry and reaction mechanism are same as on GCE.

❖ At PPy/GCE

This part deals with the electrochemical studies of the six drugs using polypyrrole film deposited glassy carbon electrode. The polypyrrole was deposited on glassy carbon
electrode and reproducible films were obtained. Cyclic voltammetric studies of six drugs at PPy/GCE were tried. But there was small change in all drugs the cyclic voltammograms was mentioned.

The simple oxidation reaction of all the drugs at PPy/GCE was as in the bare glassy carbon electrode. The peak current was correlated as in the previous case. All the six drugs exhibited diffusion controlled irreversible reaction. The oxidation peak potential of drugs in this modified system is lower than on bare GCE systems.

Hence PPy/GCE modified electrode was chosen as the suitable electrode system. The peak currents and potential were correlated with scan rate as in previous cases. All the drugs showed diffusion controlled irreversible electrode reaction. Other electrochemical studies such as chronocoulometry and controlled potential coulometry and reaction mechanism are same as on bare GCE and other modified systems.

- **At MWCNTs/GCE**

1. Cyclic voltammetric studies were carried out using MWCNTs/GCE successfully at pH 13.0 for all drugs.

2. It was found that all six drugs showed cyclic voltammetric behaviour similar to that shown by GCE, NaMM and PPy modified system.

3. The cyclic voltammetric behaviour of drugs on bare GCE and modified electrodes were compared. The comparison was made for the cyclic voltammetric results obtained for drugs in suitable pH media. It has been clearly understood that MWCNTs /GCE exhibited a remarkable change for all drugs as compared with other electrode systems. All the six drugs shows higher current respons than other systems.

   This system showed lesser peak potential compared with other electrode systems. Cyclic voltammotric behaviour of drugs on various electrode systems is used. The overall
resulted bar diagram of peak current vs drugs was understood at various electrode systems (Fig. 1).

![Bar diagram of peak current vs drugs](image)

**CHAPTER VI**

**ELECTROANALYSIS OF DRUGS**

In this chapter, the details of studies made for the development of electroanalytical procedure for the determination of the four drugs is presented. Differential pulse stripping voltammetry (DPSV) was employed. The results from the previous chapters allowed us to select a suitable pH for the electroanalysis on all four electrode systems. The compound accumulation on electrode surface was studied through SEM analysis. Optimum experimental conditions were arrived by varying the parameters such as accumulation potential, accumulation time, initial potential, pulse height, pulse width and scan increment. The peak current was measured under optimum conditions at various concentrations. Calibration plot was arrived at DPSV. The limits of determination and standard deviation in percentage for six measurements were arrived at.

All these results are presented in the following:
Working electrodes: GCE, NaMM/GCE, PPy/GCE and MWCNTs/GCE

Differential pulse stripping voltammetric behaviour of drugs was carried out on various electrode surfaces. The best response was exhibited in MWCNTs/GCE for all six drugs. The optimum experimental condition is presented in table 1.

The above studies revealed that DPSV is a better method for the determination of these drugs. The suitability of the proposed method was verified by determining the concentration of the pharmaceutical and urine samples.

Thus this piece of investigation leads to establishing the redox mechanism of drugs in bare GCE and modified GCE systems and proposing suitable electroanalytical method for the determination of these drugs.
Table 1. Optimum experimental conditions arrived in DPSV on MWCNTs /GCE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Range studied</th>
<th>Optimum value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AMLD</td>
<td>FELD</td>
</tr>
<tr>
<td>pH</td>
<td>1.0-13.0</td>
<td>1.0-13.0</td>
</tr>
<tr>
<td>Accumulation potential (V)</td>
<td>-0.1 to 0.4</td>
<td>-0.1 to 0.4</td>
</tr>
<tr>
<td>Accumulation time (Sec)</td>
<td>10-60</td>
<td>10-60</td>
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<tr>
<td>Initial scan potential (V)</td>
<td>-0.4 to 0.2</td>
<td>-0.4 to 0.2</td>
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<tr>
<td>Pulse Height (PH) (mV)</td>
<td>25 to 150</td>
<td>25 to 150</td>
</tr>
<tr>
<td>Pulse width (PW) mSec</td>
<td>25 to 150</td>
<td>25 to 150</td>
</tr>
<tr>
<td>Scan Increment (SI) mV</td>
<td>2 to 20</td>
<td>2 to 20</td>
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<tr>
<td>Stirring rate (rpm)</td>
<td>50 to 250</td>
<td>50 to 250</td>
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<tr>
<td>Rest period (Sec)</td>
<td>2 to 10</td>
<td>2 to 10</td>
</tr>
<tr>
<td>Studied conc. range (μg/mL)</td>
<td>0.01 to 0.3</td>
<td>0.01 to 0.3</td>
</tr>
<tr>
<td>LOD(μg/mL)</td>
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<td>0.005</td>
</tr>
<tr>
<td>% of RSD</td>
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<td>2.7</td>
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</table>