# Electrochemical Reduction of Nicardipine

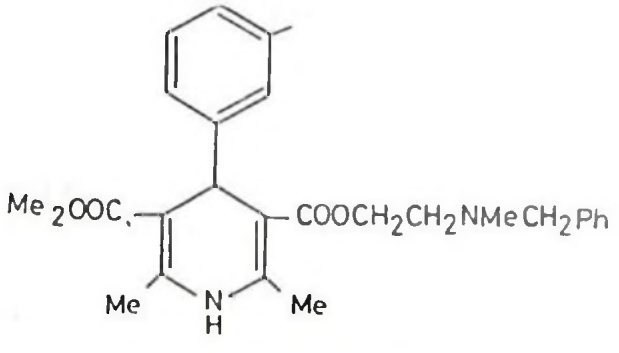
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The Electrochemical reduction behaviour of Nicardipine has been studied in different supporting electrolytes in methanol-water mixtures by employing DC polarography, cyclic voltammetry, controlled potential electrolysis and millicoulometry. The kinetic parameters such as diffusion coefficient (D) and heterogeneous forward rate constant ($k^0_h$) values are evaluated and reported.

Nicardipine [I] [2-(N-methyl-benzyl-amine) ethyl methyl-1,4 - dihydro-2,6-dimethyl-4(3-nitrophenyl) pyridine 3,5-dicarboxylate] is a vasodilator which is claimed to improve cerebral circulation [1]. It is indicated in the basic treatment of essential arterial hypertension [2-4]. The bioavailability was studied by Kato [5]. Takenaka et al [6] had analysed the pharmaceutical dosage of nicardipine.

I Nicardipine ($R\text{-}NO_2$); where R =




The reduction of nicardipine has been studied in methanol over a wide pH range employing different techniques such as cyclic voltammetry, DC polarography, AC polarography, differential pulse polarography, controlled potential electrolysis and millicoulometry to understand the reduction mechanism.

## EXPERIMENTAL

The supporting electrolytes ranging from pH 2.0 to 12.0 were prepared by using 0.2 M boric acid, 0.05 M citric acid and 0.1 M trisodium orthophosphate. All experiments were carried out at 28±1 °C. The stock solution of the drug was prepared in methanol. The apparatus and measurement are the same as reported earlier [7].

## RESULTS AND DISCUSSION

Nicardipine exhibits a single well defined wave/peak in all the buffer systems studied over the pH range 2.0 to 12.0. Typical voltammograms are given in Fig.1-3. The plots of $i_d$ *vs* $h^{1/2}$ (DC), $i_m$ *vs* $t^{2/3}$ (AC) and $i_p$ *vs* (scan rate)$^{1/2}$ (CV) were found to be linear and pass through origin. This indicates that the reduction process is diffusion controlled and adsorption free.



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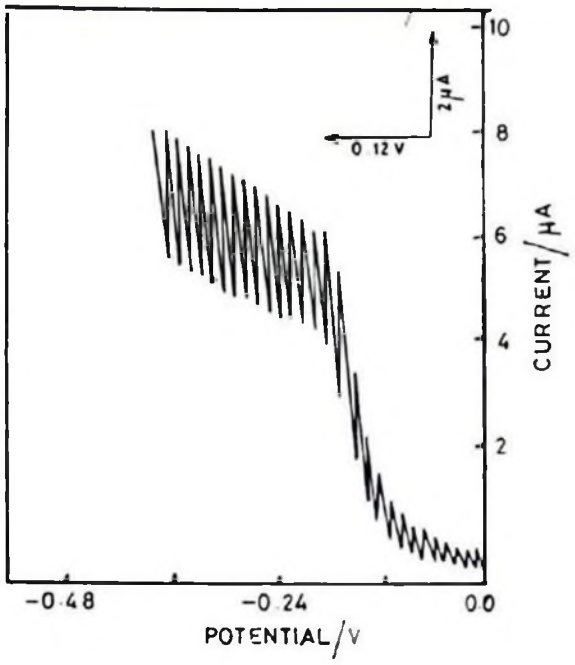



**Fig. 1 Typical DC polarogram of nicardipine**
pH 2.0; Concentration 0.5mM; Drop time 3 sec

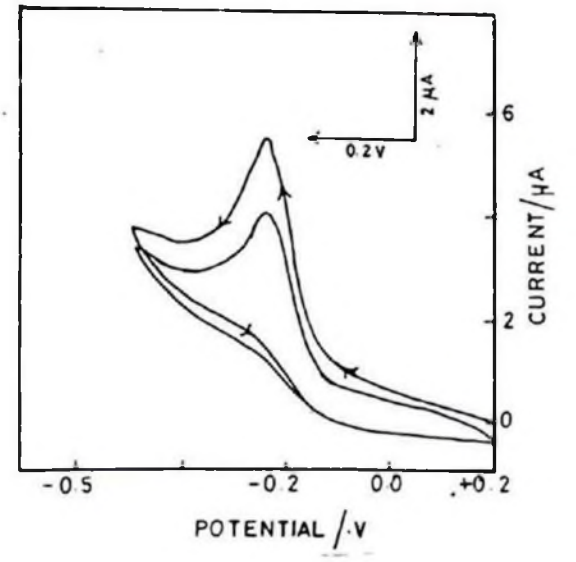



**Fig.2 Typical cyclic voltammogram of nicardipine**
pH 4.0; Concentration 0.5mM; Scan rate 60mV/sec

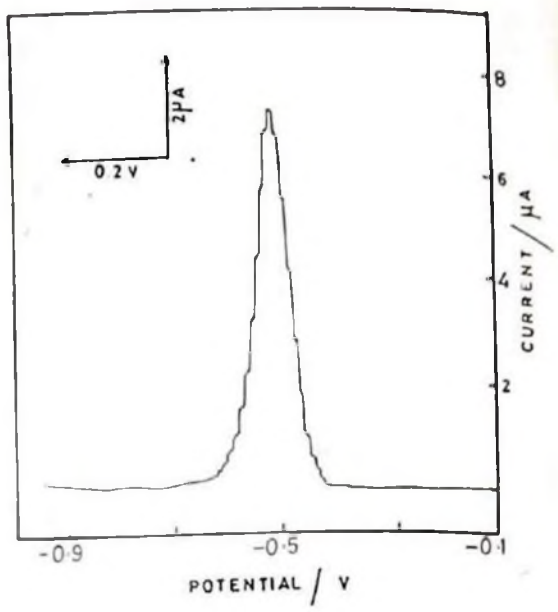



**Fig.3 Typical differential pulse polarogram of nicardipine**
pH 10.0; Concentration 0.5mM; Drop time 2sec.

A plot of $E_{dc}$ *vs* $\log[i/(i_d - i)]$ is linear and results in a slope > 59.2/n mV. The values of potentials $E_{1/2}$, $E_p$, $E_s$ and $E_m$ of nicardipine are observed to shift towards more negative values with increasing concentration of the depolariser. The plot between $i_m$ *vs* $(1-\sigma)/(1+\sigma)$ (from CV) is found to be non linear and AC polarographic summit potential is observed to deviate from the DC polarographic half-wave potential. All these indicate the electrode process to be irreversible.

Millicoulometry (both at pH 2.0 and 4.0) gave the value of the number of electrons as four. Controlled potential electrolysis is carried out at -0.26 V *vs* SCE in pH 2.0; the product is identified through I.R. spectral studies (Nujol: 3400 $cm^{-1}$

to 3250 $cm^{-1}$ and 1600 $cm^{-1}$). This indicates the final product to be a hydroxylamine.

The reduction step is ascribed to the four electron reduction of the nitro group giving corresponding hydroxylamine. A small anodic peak ($a_1$) has been observed in the reverse scan of cyclic voltammogram at pH > 10. In the second forward scan, another small cathodic peak ($c_2$) is noticed at more positive potentials than ($c_1$). The anodic peak ($a_1$) may be due to the oxidation of hydroxylamine formed at ($c_1$) to nitroso derivative and the cathodic peak ($c_2$) may be attributed to the reduction of the nitroso derivative to the hydroxylamine [8]. The relevant electrode process related to the above peaks are illustrated below

Peak $C_1$ : $R—NO_2 + 4e^- + 4H^+ \longrightarrow R—NHOH + H_2O$

Peak $a_1$ : $R—NHOH \longrightarrow R—NO + 2e^- + 2H^+$

Peak $C_2$ : $R—NO + 2e^- + 2H^+ \longrightarrow R\text{-}NHOH.$

The various kinetic parameters of the electrode process such as diffusion coefficient and heterogeneous forward rate constant values evaluated from the different techniques are given in Table 1.

**Table 1**

| pH | 2.0 | 4.0 | 6.0 | 8.0 | 10.0 | 12.0 |
|---|---|---|---|---|---|---|
| **DC Polarography Drop time : 3 sec.** | | | | | | |
| $E_{1/2}$ | 0.16 | 0.25 | 0.40 | 0.47 | 0.56 | 0.63 |
| $Dx10^6$ | 3.27 | 2.21 | 2.12 | 2.07 | 2.01 | 1.91 |
| $k^0_h$ | $9.32x10^{-4}$ | $3.54x10^{-5}$ | $9.52x10^{-6}$ | $8.93x10^{-8}$ | $4.79x10^{-10}$ | $2.93x10^{-11}$ |
| **Cyclic Voltammetry** | | | | | | |
| $E_p$ | 0.14 | 0.23 | 0.39 | 0.45 | 0.49 | 0.58 |
| $Dx10^6$ | 2.57 | 2.41 | 2.19 | 2.11 | 2.02 | 1.98 |
| $k^0_h$ | $9.96x10^{-4}$ | $9.65x10^{-5}$ | $6.37x10^{-6}$ | $9.27x10^{-8}$ | $3.63x10^{-10}$ | $1.29x10^{-11}$ |
| **AC Polarography** | | | | | | |
| $E_a$ | 0.17 | 2.25 | 0.41 | 0.46 | 0.55 | 0.61 |
| $Dx10^6$ | 2.21 | 2.10 | 2.01 | 1.89 | 1.82 | 1.76 |
| $K_a$ | $9.53x10^{-2}$ | $3.78x10^{-3}$ | $9.97x10^{-5}$ | $5.43x10^{-6}$ | $9.92x10^{-6}$ | $3.71x10^{-7}$ |
| **Ring Disc Electrode** | | | | | | |
| $E_m$ | 0.12 | 0.25 | 0.38 | 0.44 | 0.54 | 0.58 |
| $Dx10^6$ | 2.68 | 2.52 | 2.35 | 2.16 | 2.11 | 2.06 |
| $k^0_h$ | $6.78x10^{-4}$ | $2.93x10^{-5}$ | $6.84x10^{-6}$ | $2.63x10^{-8}$ | $2.73x10^{-10}$ | $1.39x10^{-11}$ |

The reason for slight variation in diffusion coefficient values with increase in pH may be attributed to the less availability of protons [9] with increase in pH.

**Analysis**

In the present investigation differential pulse polarography has been employed for the quantitative estimation of the nicardipine adopting both calibration and standard addition methods. The polarographic peak obtained in the pH region 4.0 < pH < 6.0 is well resolved and may be utilised for the analysis. The technique is used to determine the nicardipine over the concentration range $2.4 \times 10^{-5}$ M to $2.6 \times 10^{-7}$ M. The optimum conditions for the analytical determinations of nicardipine in pH 4.0 is found to be a drop time of 2 sec and pulse amplitude of 60 mV and an applied potential of -0.23 V *vs.* Ag/AgCl (S), Cl-

The analytical procedure recommended is as follows: $1.5 \times 10^{-5}$ M standard solution is prepared by dissolving the required quantity of nicardipine in methanol. 1 ml of standard solution is placed in a polarographic cell and is made up with 9 ml of supporting electrolyte and then deaerated with oxygen - free nitrogen gas for 10 minutes. After recording the polarogram, small increments (0.2 ml) of the standard solution is added and after deacration for one minute, the polarogram is again recorded under similar conditions. In the same manner, 10 polarograms are recorded after 10 standard additions. Calibration graph is found to be linear. The results obtained with the above procedure are accurate and reproducible. The relative standard deviation values and correlation coefficient (for 10 replicants) are found to be 2.3 % and 0.994 for nicardipine.

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