Available online at www.ijpsdr.com
International Journal of Pharmaceutical Sciences and Drug Research 2011; 3(3): 253-255

Research Article ISSN 0975-248X

Differential Pulse Polarographic Determination of Nifedipine in Pharmaceutical Formulations

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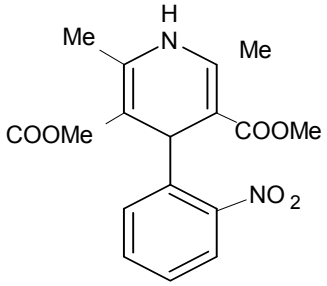
ABSTRACT
A simple and rapid differential pulse polarographic method has been developed for the trace determination of Nifedipine. A well-defined single peak with Ep value of -0.51 V is obtained in 0.1M acetate buffer (pH 5.0). The linearity is valid up to 5×10^{-5} M *(*r =0.9995) with minimum detection limit of 3.5×10^{-8} M. Precision of the method developed is implied from the values of relative mean deviation, standard deviation and coefficient of variation, which are 2.05%, 1.1 and 3.2% respectively. Marketed formulations of Nifedipine have been analyzed by calibration and standard addition methods. Recovery experiments have been found to be quantitative and analysis to determine the mass per tablet is obtained within ± 0.2% of the expected value. The studies have shown that the method is simple, reproducible and accurate and can be used in the analysis of marketed formulations.

Keywords: Differential pulse polarography, Nifedipine, pharmaceutical.

INTRODUCTION

3, 5-dimethyl 2, 6-dimethyl-4-(2-nitrophenyl)-1, 4-dihydropyridine-3, 5-dicarboxylate is commonly known as Nifedipine and has the following structure.



Nifedipine is a calcium antagonist containing reducible nitro group. HPLC method is being used most frequently for the trace analysis of Nifedipine. [1-2] Other instrumental techniques used for analysis of Nifedipine are spectrophotometry [3], gas chromatography [4], Spectrofluorometry [5] etc. Quantitative estimation of nifedipine has been carried out in human plasma [1-6], dog plasma [7] and cat plasma [8] by chromatographic techniques. DPAdSV studies of Nifedipine have been reported in different samples using modified carbon paste electrode. [9]

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The use of glassy carbon electrode has been suggested for linear sweep and cyclic voltammetric studies. [10] Adsorptive cathodic stripping polarographic determination of trace nifedipine has been reported with high sensitivity. [11] Anodic electrochemical behavior based on the oxidation of dihydropyridine ring to form pyridine derivative compound has been reported. [12] Photodegradation studies with differential pulse polarographic determination of Nifedipine are carried out. [13] However, the detection limit obtained by this method was found to be lower as compared to the known method. Also, linear range was found to be much wider than the reported values. The developed method has also been applied to estimate the compound in marketed formulations.

MATERIALS AND METHODS

Apparatus

Differential pulse polarographic studies of nifedipine were carried out with Metrohm Polarecord E-506 Serie-03 connected to the Metrohm polarography stand E-505. The electrode assembly consisted of the dropping mercury electrode (DME) as working electrode, Ag/AgCl (sat. KCl) as reference electrode and a platinum auxiliary electrode. Nitrogen gas was used for deaeration. Mercury was purified by agitating for about 12 h in contact with 10% nitric acid, followed by thorough washing with distilled water and further distilled under reduced pressure in a mercury distillation unit.

Reagents and solutions

All the chemicals used were of Analytical Reagent (AR) grade. The solutions were prepared in doubly distilled water. A standard solution of pure sample of Nifedipine was prepared by dissolving 0.2 g of the substance in 50 ml of dimethyl formamide (DMF) and the volume was made up to 100 ml with double distilled water (DDW). The compound was insoluble in water but found to be stable for about a week in DMF-water mixture. In the present work the solution was prepared afresh every four days. The flasks containing this solution and also the polarographic cell were covered with black paper as Nifedipine undergoes decomposition on exposure to light.

Acetate buffer of pH 5.0 was used as a supporting electrolyte and a 0.1% aqueous solution of Triton-X-100 was used to eliminate the polarographic maxima.

General procedure

An aliquot containing 30µg of Nifedipine was taken and to it was added 15 ml of the acetate buffer (pH 5.0), 0.5 ml of 0.1% Triton-X-100 and the total volume of the solution was made up to 25 ml. The solution was deaerated for 20 min with nitrogen. The polarograms were recorded with the recorder settings as given below:

Starting potential	-0.2 V	Paper speed	60 mm min^{-1}
Pulse amplitude	100 mV	Scan rate	6 mV s^{-1}
Drop time	2 s	Sensitivity	1×10^{-9} A/mm

In all cases a blank recording was first performed with the base electrolyte solution, and suitable blank correction was applied in the calculations if necessary. The experiments were repeated three times to ensure reproducibility of the results.

RESULTS AND DISCUSSION

Effect of pH

The polarograms of Nifedipine were recorded in different buffer systems. Single symmetrical peak was obtained in Britton-Robinson buffer from pH 3.0 to 10.0, acetate buffer from pH 4.0 to 6.0, borate buffer from pH 7.5 to 11.0, Mcllavaine buffer from pH 3.5 to 7.0 and Clark-Lubs buffer from pH 5.0 to 10.0. Acetate buffer at pH 5.0 was selected for all studies as a single sharp peak with high degree of reproducibility was obtained under these conditions.

Effect of pH on peak current and peak potential in 0.1M acetate buffer is shown in Fig. 1.

Effect of maxima suppressor

The effect of maxima suppressor was studied using Triton-X-100, gelatin and bromophenol blue. In the absence of maxima suppressor, the peak was highly unsymmetrical. Addition of gelatin (0.1%, 0.5 ml), bromophenol blue (0.1%, 0.5 ml) or Triton-X-100 (0.1%, 0.5 ml) improves the symmetry of the peak. With addition of 0.5 ml of 0.1% Triton-X-100, a narrow, symmetrical peak was obtained. With every 0.5 ml addition of Triton-X-100 there was about 8% decrease in the diffusion current. Hence, 0.5 ml of 0.1% Triton-X-100 was selected as the optimum concentration for further studies.

Other parameters

The diffusion current increased linearly with increase in the drop time of 0.4 to 2.0 s. At drop times above 2 s the increase in diffusion current was not linear. With increase in pulse amplitude from 20 to 100 mV, the diffusion current showed a linear increase. Thus, drop time of 2 s and pulse amplitude of 100 mV was selected for further studies.

Reversibility

A graph of E versus log (I/I_d - I) from a DC polarogram showed that it was a diffusion controlled process. A series of DC polarograms were recorded at varying concentrations and $E_{1/4}$ -$E_{3/4}$ was calculated which was found to be greater than 56 mV. The value of slope calculated from the graph of E versus log (I/I d -I) was greater than 59.2 mV. In differential pulse mode, the graph of Ip versus $\nu^{1/2}$ (ν = scan rate) did not pass through the origin, and the value of Ep also showed a change with a change in drop time. This implied that the reaction taking place at the electrode was irreversible. [14]

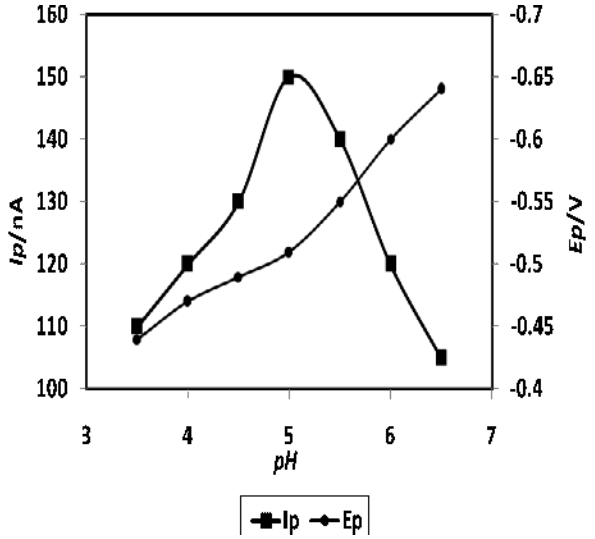

Fig. 1: Effect of pH on peak current (Ip) and peak potential (Ep)

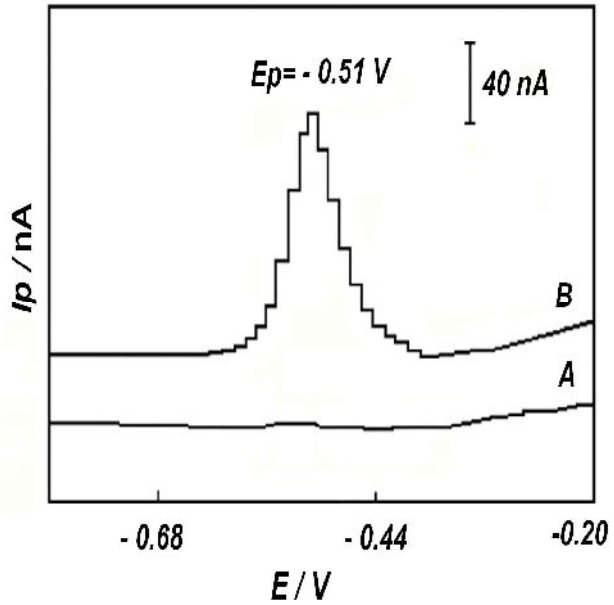

Fig. 2: Typical voltammogram of (A) 0.1 M Acetate buffer with pH 5.0 and (B) with 20µg Nifedipine

Calibration and validation

A linear calibration plot was obtained from 5.0×10^{-7} M to 5.0×10^{-5} M of Nifedipine with equation of regression line **y**(nA)=52.3**x**(µM)–2.61 and coefficient of correlation 0.9997

indicating high degree of current-concentration linearity in this range. The Ep value obtained was in the range of -0.47 to -0.60 V, which is attributed to the reduction of nitro group. [12-13] The lowest determinable limit of Nifedipine was found to be 3.5×10^{-8} M. The detection limit is comparable with those obtained by HPLC [2], spectrophotometric [3] and cathodic stripping polarographic methods. [11]

Relative mean deviation (RMD), standard deviation (SD) and coefficient of variation (CV) were calculated for 10 repetitive recordings for 1.0×10^{-7} M Nifedipine solution. These values were found to be 2.05%, 1.1 and 3.5% respectively. A typical polarogram obtained under optimum conditions is shown in Fig. 2.

Application

The utility of the method developed was seen by its application to the determination of Nifedipine in tablets as well as capsules. Twenty tablets/ capsules of the drug samples were weighed and finely powdered. The powder was weighed accurately, dissolved in 50 ml DMF and kept overnight. The solution was filtered and made up to 100 ml with double distilled water. Different aliquots of this solution were analyzed using calibration curve and standard addition methods. The results obtained by these methods are shown in Table 1.

Table 1: Determination of Nifedipine in pharmaceutical formulations

Drug sample	Volume of drug sample added (µl)	Ip (nA)	Amount of nifedipine (ppm) Expected	Observed*
Nifedipine Tablet	25	52	0.40	0.36 ± 0.02
	50	116	0.80	0.78 ± 0.04
	75	180	1.20	1.20 ± 0.03
	100	240	1.60	1.61 ± 0.04
	125	300	2.00	2.00 ± 0.04
Nifedipine Capsule	25	64	0.40	0.44 ± 0.02
	50	128	0.80	0.86 ± 0.05
	75	180	1.20	1.20 ± 0.07
	100	236	1.60	1.56 ± 0.04
	125	296	2.00	1.98 ± 0.03

*(Avg ± SD) of 3 observations

Recovery experiment

To determine the percentage recovery, a fixed quantity of Nifedipine sample solution was taken and to it was added three different (5, 10 and 15µg) levels of working standard Nifedipine. At each level the polarograms were recorded seven times and the amount of Nifedipine was computed using the formula:

$$Percentage\ \ recovery = \frac{N\left(\sum XY\right)-\left(\sum X\right)\left(\sum Y\right)}{N\left(\sum X^2\right)-\left(\sum X\right)^2}\times 100$$

Where N is the number of observations, X is the amount of drug added and Y is the amount of drug obtained. The same procedure was adopted for both the marketed samples of Nifedipine at two different initial concentrations. The average percentage recovery for tablet was 100.99% and for capsule was 101.82%.

ACKNOWLEDGEMENT

The authors are grateful to the Alexander von Humboldt Foundation of Germany for the donation of the Metrohm Polarograph and to Department of Pharmacy, Nagpur University, Nagpur, India for providing the drug sample.

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