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DIFFERENTIAL PULSE ADSORPTIVE STRIPPING VOLTAMMETRIC DETERMINATION OF NIFEDIPINE IN DRUG BY USING HANGING MERCURY DROP ELECTRODE

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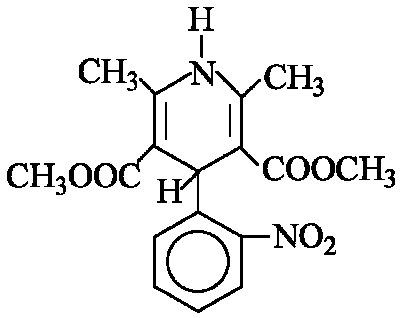
ABSTRACT

Nifedipine is a calcium - channel antagonist drug used in the management of angina pectoris and hypertension through inhibition of calcium influx. A simple, rapid, and selective differential pulse adsorptive stripping voltammetric method based on reduction of an aromatic nitro group in the drug onto hanging mercury drop electrode, that has been developed for the determination of nifedipine. The analytical parameters effect the electrode reduction process have been studied such as pH, accumulation time, accumulation potential, pulse amplitude, frequency, temperature. The results show that: at pH 4; accumulation time to obtain maximum current is 30s, 120s and 300s for 10^{-6} M, 10^{-7} M and 10^{-8} M, respectively; pulse amplitude 50 mV; sweep rate 12.5 mV/s. The peak current showed a linear relationship with concentration in the range 10^{-8}M - 10^{-7} M. The method was applied succesfully for the direct determination of nifedipine in drugs.

I - INTRODUCTION



Nifedipine [1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylate is one of the first generation of calcium-channel blockers. It is a dihydropyridine that does not resemble structurally other calcium antagonists.

Several analytical methods have been described for the assay of nifedipine in pharmaceutical formulations. These methods include spectrophotometry, gas chromatography, liquid chromatography, high-performance thin-layer chromatography, high-performance liquid chromatography (HPLC), polarography, linear-sweep voltammetry and differential-pulse stripping voltammetry. The electroanalytical methods are highly sensitive and selective, simple, easy to use and low cost. On the other hand, adsorptive stripping voltammetry is an important analytical technique for determination of a wide range of electroactive pharmaceutical compounds which can be adsorbed onto the surface of the working electrode, specially the hanging mercury drop electrode (HMDE) [1 - 4].

In this paper, a differential pulse adsorptive stripping voltammetric method (DPAdSV) has been applied for the determination of nifedipine in drugs.

II - EXPERIMENTAL

2. Reagents

A standard stock solution of 10^{-2} mol/l nifedipine was prepared in methanol.

Standard solutions were prepared daily by further dilution of the standard stock solution with methanol : water (1:2) to produce 10^{-4}mol/l and 10^{-6}mol/l nifedipine solutions. The standard stock and the working solutions were kept in dark bottles immediately after preparation and stored at 4°C.

Bristton–Robinson (BR) buffers of pH 2-12 (mixtures of 0.04 mol/l acetic, orthophosphoric, and boric acids; adjusted to the required pH with 0.2 mol/l sodium hydroxide solution) were prepared and used as supporting electrolytes. All reagents were of analytical grade.

2. Apparatus

All measurements were performed with an µAutolab type III (the Netherlands) and a hanging mercury drop electrode (VA 663, Metrohm, Switzerland), controled by software 757 VA computrace. The reference electrode (Metrohm, Switzerland) was a double-junction Ag/AgCl electrode with 3M KCl in the salt bridge, and the counter electrode (Metrohm, Switzerland) was a glassy carbon rod. All measurements were carried out in solutions which were thoroughly deaerated with high-purity nitrogen for at least 5 min.

III - RESULTS AND DISCUSSION

1. Cyclic Voltammetric studied

Figure 1, shows cyclic voltammogram for 10^{-6} M nifedipine in 0.04 M Britton-Robinson (BR) buffer solution at pH 4, accumultion time 30s, accumulation potential 0V. When scanning from potential 0 to -1.2V (Vs. Ag/AgCl), nifedipine yielded one peak, which was due to the reduction of the nitro group and no peak was observed on the anodic branch, indicating that the reduction of nifedipine is irreversible.

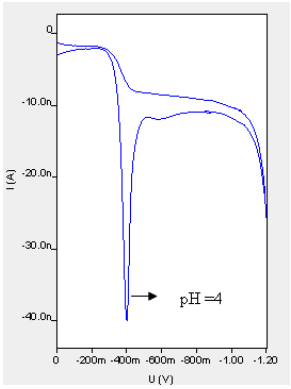


Figure 1: Cyclic Voltammogram of 10^{-6} M nifedipine in BR buffer of pH = 4

2. Differential Pulse Adsorptive Stripping Voltammetry

a) Effect of pH

Figure 2, shows that, the influence of pH on the peak current (i_p) at 10^{-6} M of nifedipine. The peak current increases gradually with the increase of pH of the solution until it reaches the maximum value at pH 4.0; However, for pH values higher than 4, peak current decreases. A shift of peak potential toward a more negative value was observed as the pH was increased and linearly with pH of 2-11 according to the equation E_p = 0.212 + 0.0497.pH, Which indicated the existence of a protonation reaction for the reduction of nifedipine.

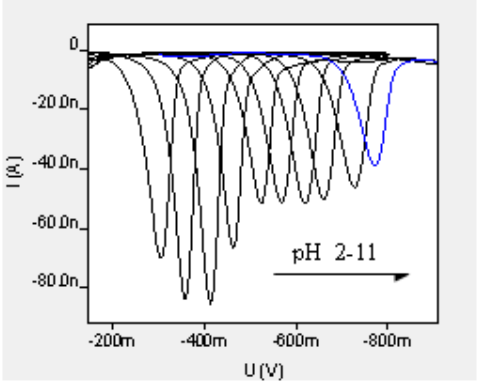


Figure 2: Cathodic adsorptive differential pulse voltammograms for 10^{-6}M nifedipine in BR buffers of different pH, E_{acc} = 0V, t_{acc}= 30s

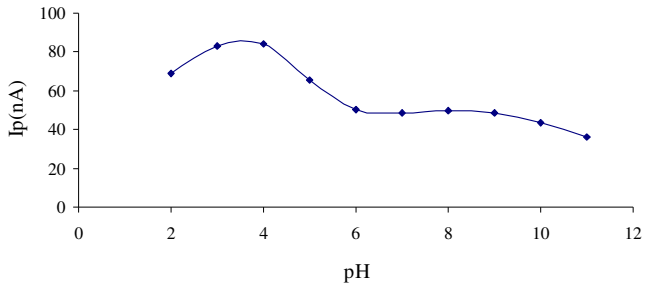


Figure 3: Effect of pH on the DPAdSV response of 10^{-6}M niedipine

The experimental results showed that the shapes of curves were nearly the same in some buffers such as acetate, phosphate. However, the current intensity in the BR buffer is higher than that in acetate and phosphate buffers. A BR buffer of pH 4.0 was chosen with respect to a sharper response for analytical applications. A 0.04 M concentration of the buffer was selected to obtain an adequate buffering capacity.

b) Effect of Accumulation Potential (E_{acc})

The effect of an accumulation potential (E_{acc}) on the adsorptive stripping peak current of nifedipine was investigated after a preconcentration time of 30s at HMDE. The highest peak current was achieved at potential of -0.2 V. For the potentials higher than -0.2 V, the peak currents started decreasing. Hence, the accumulation potential of -0.2 V was used throughout the present study.

c) Effect of Accumulation Time (t_{acc})

The effect of stripping peak currents on the accumulation time period was investigated in BR buffer of pH 4.0 for 10^{-6} M, 10^{-7} M and 10^{-8} M nifedipine. Maximum peak current observed when accumulation time is 30s, 120s and 300s, respectively. The stripping signal at HMDE electrode increased linearly with an increase in the accumulation time up to maximum current. As the time became longer, the peak current did not increase showed linearity and gradualy decreased, indicating that nifedipine has adsorbed multi-coated on the HMDE so chosing suitable accumulation time is very necessary.

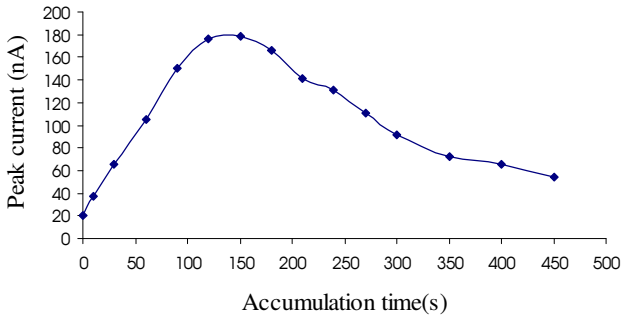


Figure 4: Effect of accumulation time on the peak current at nifedipine 10^{-7}M, pH = 4, E_{acc} = - 0.2V

d) Effect of temperature

Temperature is one of the important parameter effecting to adsorb process of nifedipine on the HMDE. The effect of temperature from 8°C to 60°C was studied with

conditions: nifedipine concentration 10^{-6} M, accumulation potential -0.2 V, accumulation time 30s, equal time 5s, pulse time 0.04s, pulse amplitude 0.05 V, voltage step 0.005 V, and sweep rate 12.5 mV/s. Fig. 5, showed that when temperature increase peak potential shift toward a more positive and peak current was high from 28°C to 35°C because of increasing temperature, proton reaction occur more easier so peak potential shifted to more positive. However, when temperature increase, adsorptive process decrease so peak current decrease when temperature increase higher 35°C.

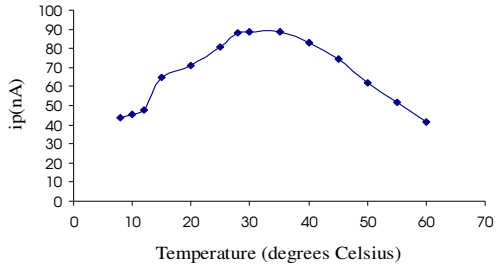


Figure 5: Effect of temperature on the peak current

e) Effect of Other Parameters

Scan rates, stirring rate, pulse amplitude, and rest period were optimized. It was found that these parameters have pronounced effects on the peak current response, so the working conditions decided upon were a stirring rate of 2400 rpm, a scan rate of 12.5 mV/sec, and a pulse amplitude of 50 mV, drop size 4. When the scan rates and pulse amplitude were increased, peak current increased but peak width increased. So scan rate of 12.5 mV/sec and pulse amplitude of 50 mV were found to be suitable for experimental studies.

f) Calibration Studies by DPAdSV

To determine nifedipine in some drugs, the linear dependence of the peak current on the nifedipine concentration was investigated. The calibration graph was linear from 10^{-8}M to 9.10^{-8} M. Calibration curve equation y = 0.315 + 5.18 x, Correlation coefficient 0.9992 and standard deviation 0.698.

Reproducibility was evaluated by performing six measurements on a 10^{-7}mol/l solution after 120s accumulation time, respectively. A mean value of 57.05 nA was found with a range of 55.0 - 58.1 nA and a relative standard deviation of 2.13%.

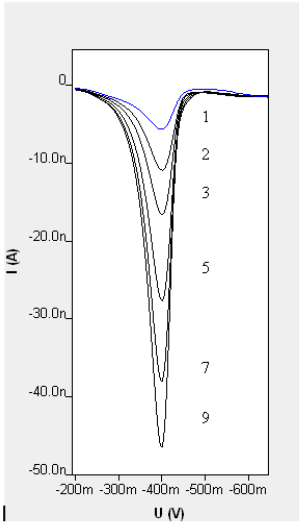


Fig 6: The effect of nifedipine concentrations (1 ÷ 9) 10^{-8} M on the peak current obtained in Britton-Robinson buffer pH 4.0 at accumulation potential -0.2 V, accumulation time 120s , pulse amplitude 50mV, pulse time 0.04 V, sweep rate 12.5 mv/s

g) Determination of Nifedipine in drugs

The proposed procedure was successfully applied for the determination of nifedipine in the drug tablets. A tablet was finely ground in an agate mortar, put powder into 100 ml volume flask, add 20 ml methanol, shake about ten minutes then dilute to volume 100ml with water, after that the mix solution was filtered through a 0.4µm with Millipore filter (Gelman, Germany). A volume of 2ml of the filtrate in a 100ml volumetric flask was dilute with double water. Take 1ml that solution into 25 ml volumetric flask containing 10ml BR buffer, an aliquot was then transferred to a

voltammetric cell. The different pulse was record, and nifedipine concentration in drug was determined by a standard method. The results are presented in table 1.

Table 1: Analytical results of some drug samples by DPAdSV

Samples	Labeled amount, mg	Average amount found, mg	Recovery percentage	RSD, %
Nifedipine stada	10	11.2	112.0	1.21
Trafidine	10	10.7	107.0	1.78
Nifehexal retard	20	21.4	107.0	1.44

IV - CONCLUSION

Differential pulse adsorptive stripping voltammetric method developed in this study is sensitive, selective, accurate, precise, cheap and easy to use for the determination of nifedipine in drug. The procedure was simple and precise; it did not spend much time to treat drug samples.

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PHƯƠNG PHÁP VON-AMPE HÒA TAN HẤP PHỤ XUNG VI PHÂN XÁC ĐỊNH NIFEDIPIN TRONG THUỐC SỬ DỤNG ĐIỆN CỰC GIỌT THỦY NGÂN TREO (HMDE)

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Tóm tắt: Nifedipin là thuốc chẹn kênh calci thuộc nhóm dihydropyridin, có tác dụng chống cơn đau thắt ngực, chống tăng huyết áp. Có nhiều phương pháp xác định nifedipin tuy nhiên phương pháp von-ampe hòa tan hấp phụ xung vi phân có độ nhạy, độ chọn lọc, độ chính xác cũng như độ lặp lại cao, đặc biệt chi phí cho phân tích thấp hơn, nhanh và đơn giản hơn. Nguyên tắc của phương pháp dựa vào sự khử của nhóm nitro vòng thơm tạo thành dẫn xuất hydroxylamin trên điện cực giọt thủy ngân treo. Các điều kiện ảnh hưởng đến quá trình khử trên điện cực đã được nghiên cứu như pH, thế tích lũy, thời gian tích lũy, biên độ xung, tốc độ quét, nhiệt độ. Kết quả cho thấy, với pH là 4, thời gian tích lũy để giá trị dòng đạt cực đại là 30s, 120s, 300s tương ứng với các nồng độ 10^{-6}M, 10^{-7}M and 10^{-8}M, biên độ xung 50mV; tốc độ quét là 12,5mV/s thì tín hiệu cường độ dòng cao, ổn định, lặp lại. Xây dựng khoảng nồng độ tuyến tính từ 10^{-8}M - 10^{-7} M. Ứng dụng thành công quy trình khảo sát được xác định hàm lượng nifedipin trong một số mẫu thuốc..