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Electrochemical behavior of anagrelide and its determination

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ABSTRACT

A simple, accurate and sensitive voltammetric method for determination of Anagrelide (ANG) using β cyclodextrin modified carbon paste electrode (CDMCPE) is developed. CDMCPE exhibited significantly increased sensitivity and selectivity for ANG compared to Carbon paste electrode. Peak currents showed a linear response in the concentration range 1.8×10^{-9} to 1.6×10^{-6} M at CDMCPE. Limit of detection (LOD) and limit of quantization LOQ were found to be 2.2×10^{-8} to 0.733×10^{-7} M with a correlation coefficient of 0.9916. The proposed method has been successfully applied for the determination of ANG in spiked serum sample, urine samples and pharmaceutical formulations.

Key words: Anagrelide, carbon paste electrode, voltammetry, pharmaceutical formulations and serum samples.

INTRODUCTION

Anagrelide [6,7-dichloro-1,5-dihydroimidazo(2,1-b)quinazolin-2(3*H*)-one] (ANG) is used to reduce elevated platelet counts and the risk of thrombosis in the treatment of hemorrhagic thrombocythemia. HPLC-MS method[1] and GC-MS[2] were reported for determination of anagrelide. The present work describes a cheaper and accurate electrochemical method for its determination at â cyclodextrin modified carbon paste electrode (CDMCPE).Several researchers have reported the application of chemically modified electrodes for the determination of drugs[3-11].

EXPERIMENTAL

Voltammograms were recorded with Metrohm 757 VA computrace (Herisau, Switzerland).The modifier β-cyclodextrin was purchased from Fluka. Paraffin oil and graphite powder (l-2um particle size) from Aldrich. Anagrelide (ANG) is purchased from Sigma. All the chemicals used for the preparation of solutions and supporting electrolytes are of reagent grade.

Recommended procedure

An appropriate amount of analyte and supporting electrolyte (BRB) is taken into 50 mL electrolytic cell and purged with oxygen - free nitrogen for 10 min. The voltammograms are recorded after small aliquot of the standard solution is added and then voltammograms recorded after each addition under similar conditions. The required accumulation potential of -0.4 V (Ag/AgCl) is then applied to the electrodes (hand made CPE or CDMCPE), with a stirring speed at 2000rpm. The stirring is stopped and after 10 sec of rest, then, the voltammograms are recorded by scanning the potential towards the negative direction using the stripping voltammetric techniques. All the measurements are performed at room temperature 21±3 V.

RESULTS AND DISCUSSION

Cyclic Voltammetry

Fig. 1 represents the cyclic voltammograms for 3.0×10^{-9} M Anagrelide in BR buffer solution of pH 3.0 at bare carbon paste electrode (CPE) and â-cyclodextrin modified carbon paste electrode (CDMCPE), with accumulation times of 300s and 150s respectively and accumulation potential of -0.4 V. On scanning from the potential 0 to -1.6 V (vs Ag/AgCl). ANG yields one peak, which is due to the reduction of the carbonyl-group[11-13] and no peak is observed on the anodic branch, indicating that the reductions of Anagrelide is irreversible. For the reduction peaks observed, the voltammetric currents at CDMCPE are higher in comparison with the bare CPE, indicating that, the CDMCPE has better efficiency for accumulating drugs.

Differential Pulse Voltammetry

Fig. 2 illustrates DPAdSV for 2.6 x 10-9 M Anagrelide with a bare CPE and b-cyclodextrin modified CPE. The higher stripping peak is observed at CDMCPE in comparison with bare CPE. The systematic studies of various experimental and instrumental parameters that affect the adsorptive stripping voltammogram response are carried out to establish the optimum conditions.

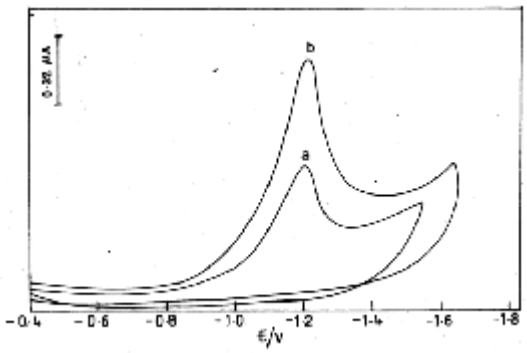


Fig. 1: Typical CV of Anagrelide at (a) at (a) bare CPE (b) CDMCPE

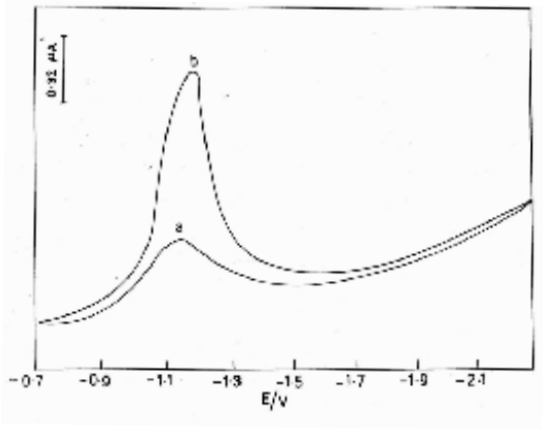


Fig. 2: Typical DPV of Anagrelide at (a) bare CPE (b) CDMCPE

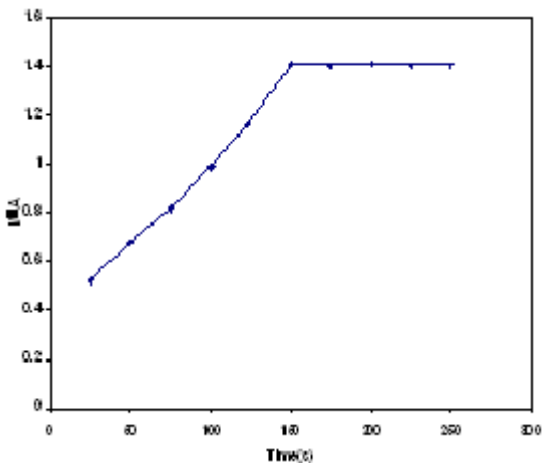


Fig. 3: Effect of accumulation time

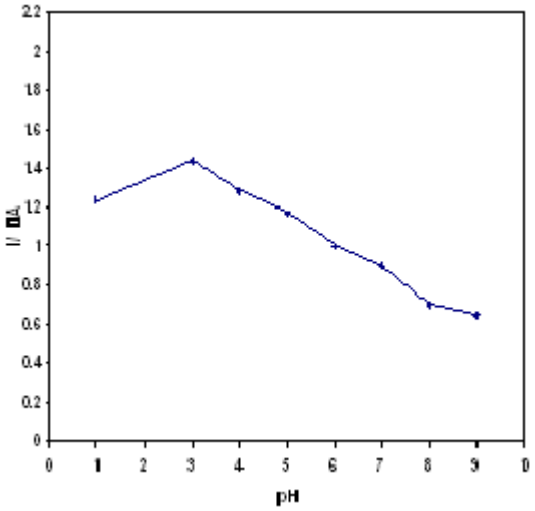


Fig. 4: Effect of pH

Table. 1: Experimental data of ANG

Parameters	Anagrelide	
	CPE	**CDMCPE**
Linearity range (M)	1.2×10^{-6} to0.8×10^{-5}	1.8 ´ 10^{-9}to1.6×10^{-6}
Calibration curve equation	Y(mA)= 0.8214 ×+ 0.0205	Y(mA)=0.4389 ×+0.06947
Correlation coefficient	0.9995	0.9916
L.O.D (M)	2.7×10^{-8}	2.2×10^{-9}
L.O.Q (M)	0.9×10^{-7}	0.733×10^{-8}
Repeatability ofpeak currents%RSD)	5.20	5.32
Repeatability ofPeak potentials%RSD)	0.74	0.81
Reproducibility of peak currents%RSD)	4.23	4.42
Reproducibility of potentials%RSD)	0.51	0.58
Numbers of assays	12	12

Table 2: Determination of ANG in Pharmaceutical Formulations

Name of the drugs	Amount labeled (m.g/L)	*Average amount found(m.g/L)	Recovery percentage (%)	±S.D	RSD
Anagrelide	2	1.95	97.5	0.030	1.538
	4	3.88	97.0	0.0450	1.0309
	6	5.95	99.16	0.02	0.336

* Each value is an average of three determinations

Table 3: Determination of ANG in Human Serum Samples

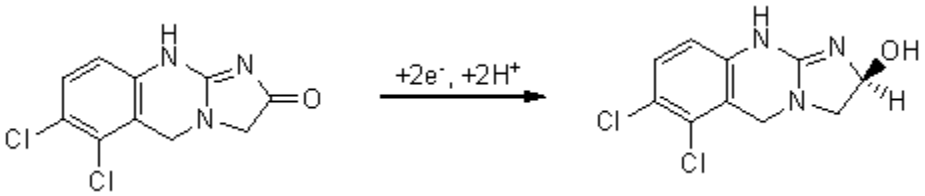
Name of the drugs	Amount labeled (m.g/L)	*Average amount found(m.g/L)	Recovery percentage (%)	±S.D	RSD
AANG	2	1.95	97.50	0.0300	1.538
	4	3.92	98.00	0.0291	0.7423
	6	5.75	95.88	0.0501	0.8713

* Each value is an average of three determinations

Table 4: Determination of ANG in spiked human urine samples

Name of the drugs	Amount labeled (m.g/L)	*Average amount found(m.g/L)	Recovery percentage (%)	±S.D	RSD
Anagrelide	2	1.96	98.0	0.0003	0.01536
	4	3.91	97.75	0.06	1.534
	6	5.96	99.33	0.0264	0.442

* Each value is an average of three determinations.



Scheme 1: Reduction of Anagrelide

This peak is attributed to the reduction of carbonyl group according to the currently accepted mechanism for the electroreduction of carbonyl compounds[14].

CONCLUSION

In the present paper a simple, accurate and precise voltammetric method was developed for the determination of ANG. The proposed method has been validated by their determination in pharmaceutical formulations, human serum samples and human urine samples. The present method has been compared with already existing methods for its determination and found better recovery, more accurate, more sensitive and achieved at lower detection limits.

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