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Differential pulse polarographic behavior of nitacrithiazole in pharmaceutical formulations and urine samples

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ABSTRACT

Electrochemical behaviour of nitacrithiazole was investigate by differential pulse polarography (DPP) using a dropping mercury electrode as working electrode and Ag/AgCl reference electrode in universal buffer of pH range from 2.0 to 12.0. Millicoulometric experiment is performed successfully in estimating the number of electrons and protons to understand reduction mechanism. The polarography study of nitacrithiazole shows that it is reduced in four electron step in acidic medium. The linearity was maintained at 1.0×10^{-5} to 1.0×10^{-9} mol dm^{-3} with detection limit of 1.7×10^{-9} mol dm^{-3}. The recovery was 98.40% to 99.80% and relative standard deviation 1.4%. The nitacrithiazole has been determined with good results by this method in pharmaceutical formulations.

KEYWORDS

Nitacrithiazole;
Differential pulse polarography (DPP);
Formulations.

INTRODUCTION

Nitacrithiazole, (4-[(4-nitroacridin-9-yl) amino]-N-(1,3-thiazol-2-yl) benzene sulfonamide) $C_{22}H_{15}N_5O_4S_2$ (Figure 1). The reduction of nitro compounds at the dropping mercury electrode in aqueous solutions is described by Shikata and coworkers[1,2]. The number of papers have been published on nitro aromatic reductions, following the early work of Geske and Maki[3]. However, the reduction mechanism for several aromatic and heterocyclic nitrocompounds was presented by Zuman and co-workers[4-12]. A survey of the literature reveals that no attempt has been made to study the electrochemical reduction behavior of nitacrithiazole as well as its determination in pharmaceutical formulations by using analytical methods to the best of our knowledge.

The aim of this study was to develop a simple and rapid method for trace analysis of nitacrithiazole in pharmaceutical formulations and urine samples by differential pulse polarography. Therefore, electrochemical behavior of nitacrithiazole in aqueous buffered media to

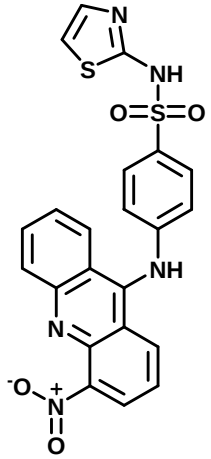

Figure 1 : Structure of nitacrithiazole

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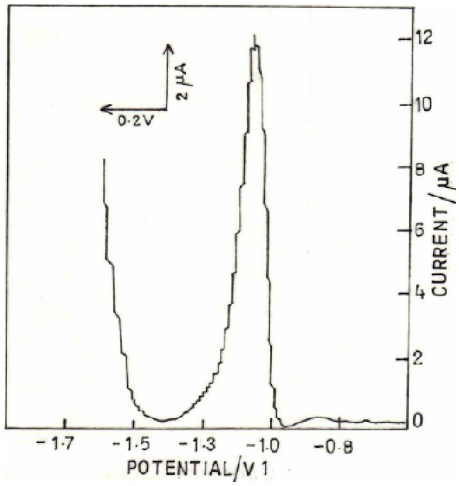


Figure 2 : Typical differential pulse polarogram of nitacrithiazole at pH 4.0 Concentration: 1.0×10^{-5} M; Pulse amplitude: 60mV; scan rate 12mV/sec; Drop time: 3 sec

arrive at the information on the mechanistic aspects and the electrode kinetics concerned and an attempt has also been made to determine the title compound in pharmaceutical formulations and urine samples by using differential pulse polarography without any prior separations.

EXPERIMENTAL

Materials

All chemicals were reagent grade chemicals (Merk, India), doubly distilled water was used in preparation of all solutions. Stock solution (1.0×10^{-3} mol dm^{-3}) was prepared by dissolving Nitacrithiazole in dimethylformamide. All dilute solutions were freshly prepared daily from the stock solution. Universal buffer solution ranging from pH 2.0 to 12.0 were prepared using 0.2M boric acid, 0.01M citric acid and 0.1M trisodium orthophosphate.

Instrumentation

Analysis were carried out with an Elico Model CL-362, three electrode system consisting of a dropping mercury electrode (DME) as the working electrode, an Ag/AgCl reference electrode and platinum counter electrode. It was outfitted with a Model LX-300^{+} X-Y recorder. All the solutions were degassed prior to analysis by bubbling purified nitrogen gas through the cell for 10 min. A detailed description of the instrumentation and experimental conditions has been reported

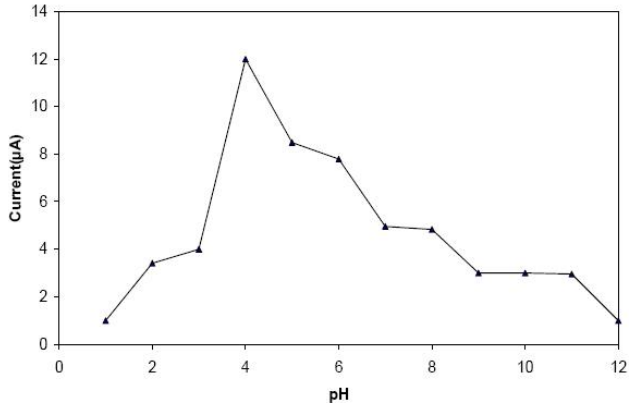


Figure 3 : Effect of pH on the peak current. Conditions as in figure 2

earlies[13]. All the experiments were performed at 25±1°C, pH measurements were carried out with a Hanna instruments (Italy) pH meter.

RESULT AND DISCUSSIONS

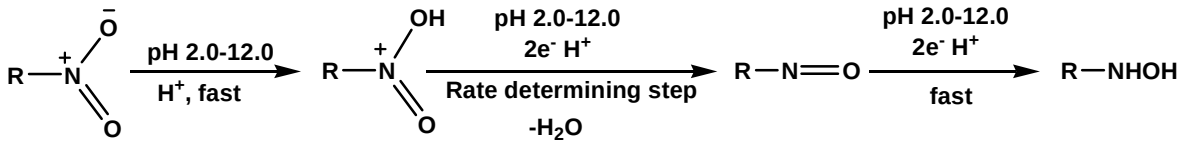
Effect of pH

The effect of pH on the pulse peak current for the reduction peak was examined using differential pulse polarography and the results are shown in figure 3. Nitacrithiazole exhibits only one peak in acidic medium and with the increase in pH-4.0, the Ep values shift towards negative direction. Therefore, pH-4.0 was selected as the optimum pH. At this pH, the sensitivity was highest, the peak was well defined, and the baseline was plat.

Nature of the electrode process

The half–wave ($E_{1/2}$) peak potential values are observed to be linear functions of pH. As the pH of the buffer system is increased, the reduction potential is found to be shifted towards more negative values[14]. The electrode processes for nitacrithiazole is found to be free from adsorption and currents are diffusion controlled in nature, which is confirmed through the linear plots of i_d vs. $h^{1/2}$ and i_m vs. $t^{2/3}$ passing through origin[15].

The technique of millicoulometry has been employed in the present investigation to evaluate the number of electrons involved in the reduction process. From the comparison of the wave heights observed, the number of electrons consumed in the over all reduction process of nitacrithiazole is found to be four in acidic as well as



Reaction Scheme 1

basic media. The electrochemical reduction process could be presented by the reaction Scheme 1.

Kinetic data

The various kinetic parameters of the electrode process such as diffusion coefficient, transfer coefficient and heterogeneous forward rate constants for nitacrithiazole from different techniques are reported in TABLE 1. The adsorption free nature of the electrode process is clearly evidenced from the nearly equal diffusion coefficient values obtained from all the techniques. The diffusion coefficient values are seen to gradually decrease which account for the decrease in diffusion current with increase in pH due to non–availability of protons. The heterogeneous forward rate constant values are found to be high in acidic media indicating the proton involvement. The rate constant values are in general found to decrease with increase in pH which indicates that the electrode reaction tends to become more and more irreversible. The number of protons involved in the rate determining step is found to be one for nitro group reduction.

The polarographic peak obtained in acidic media has been utilized in the analytical estimation of the nitacrithiazole. The main nitro group reduction peak is useful in the DPP analysis of the drugs for the following reasons: a) it occurs at small negative potentials, where a limited number of other polarographic reactions occur. Thus the determination of nitro group compounds enjoys a measure of selectivity in the field of polarographic analysis b) the peak height is relatively large because of four electron reduction step thus making polarographic determination of nitro group containing drug more sensitive involving lower detection limit of 10^{-9} mol dm^{-3} c) the peak height is unaffected by the minor changes in pH. Therefore, for analytical purpose here pH 4.0 is used.

The peak currents of nitacrithiazole are found to vary linearly with the concentration of the drug over the concentration range 1.0×10^{-5} to 1.0×10^{-9} mol dm^{-3} with the detection limit of 1.7×10^{-9} mol dm^{-3}. DPP is found to be more suitable at lower concentrations due to its high sensitivity and resolution.

TABLE 1 : Typical differential pulse polarographic data of nitacrithiazole concentration: 1.0×10^{-5} M; Drop time: 3 sec; Pulse amplitude: 60 mV

pH of the supporting electrolyte	$-E_m$ V	i_m μA	α_{na}	$D\times10^6$ Cm^2s^{-1}	$-k^\circ_{fh}$ cms^{-1}
2.0	0.18	10.4	0.32	8.44	9.86×10^{-7}
4.0	0.20	9.6	0.86	7.96	8.18×10^{-8}
6.0	0.30	9.2	0.78	7.26	2.86×10^{-9}
8.0	0.34	8.8	0.96	5.58	1.28×10^{-11}
10.0	0.38	7.6	0.88	4.72	3.60×10^{-12}
12.0	0.46	6.6	0.76	3.88	5.52×10^{-14}

Recommended analytical procedure

Standard solution (1.0×10^{-5} mol dm^{-3}) is prepared by dissolving appropriate amount of the electroactive species in DMF. A 10ml of the solution (9ml of supporting electrolyte + 1ml standard solution) is transferred into a polarographic cell and polarogram is recorded after complete deareation for 10 minutes with nitrogen gas. After getting the polarogram (Figure 2.), small increments (0.2ml) of standard solutions are added and polarograms are recorded after each addition under the same experimental conditions. The optimum conditions for the estimation of nitacrithiazole at pH 4.0 are found to be a drop time of 3 seconds, pulse amplitude of 60mV and applied potential of -1.2V vs. Ag/AgCl(s), Cl^-. The relative standard deviation and correlation coefficient values for 10 replicants are 1.58% and 0.988 respectively.

Nitacrithiazole in pharmaceutical formulations containing 245 mg in total tablet mass of approximately 250 mg has been analysed in order to examine the applicability of the method. About 10 tablets were mixed uniformly and portions equivalent to 10, 20, 30 and 40 mg of compound were accurately weighted, dissolved in pure DMF and transferred in to 25ml calibrated flasks. Aliquot of 0.5ml clear supernatant liquid was made upto 10ml with the supporting electrolyte (pH

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TABLE 2 : Determination of nitacrithiazole in pharmaceutical formulations by differential pulse polarography, Concentration: 1.0×10^{-5}M; Drop time: 3 sec; Pulse amplitude: 60 mV

Name of the formulation	Labeled amount(mg)	Amount found(mg)	Recovery (%)	Standard deviation	(%) RSD
Nitacrithiazole	5	4.92	98.40	0.04	0.4
	10	9.98	99.80	0.02	0.1
	15	14.83	98.80	0.03	0.7

TABLE 3 : Determination of Nitacrithiazole in urine samples by differential pulse polarogarphy, Concentration: 1.0×10^{-5} M; Drop time: 3 sec; Pulse amplitude: 60 mV

Sample	Labeled amount (mg)	Amount found (mg)	Recovery (%)	Standard deviation	(%)RSD
1	2.0	1.95	97.50	0.03	0.4
2	4.0	3.89	97.25	0.05	0.5
3	6.0	5.99	99.83	0.01	0.1

4.0) and polarogram recorded. The amount of the compound in portion of the sample taken was estimated by reference to calibration plot. The recovery was found to be in the range of 98.40% to 99.80% the assay results are given in TABLE 2.

The reliability of the method for the determination of nitacrithiazole in urine was checked by using different spiked urine samples in conjunction with the standard addition method. Three different urine samples were spiked with standards in concentration range at which the unchanged drug is excreted. The recovery was found to be in the range of 97.25% to 99.83% with the relative standard deviation of 0.96%. The results are given in TABLE 3.

Urine samples were obtained from the patients at a specific time intervals during single dosage administration. It is known that the portion of an orally administered dose that excreted unchanged in urine is dose dependent. However, it was observed that, after administration of single oral dose of 250mg, the drug concentration in urine increases until it reaches 12% of the initial dose at 4 hrs and then begins to decrease. Nearly 20-25% of a dose is excreted within 7 hrs. After 12 hrs, the polarographic signal disappears and the unchanged drug excreted below the method of detection of the method together with polarographically inactive nitacrithiazole. From the foregoing discussion, it has been demonstrated to be applicable to variety of samples including pharmaceutical formulations and urine samples.

CONCLUSION

The proposed method is experimentally convenient and sensitive for the determination of nitacrithiazole using differential pulse polarography on DME. This method was successfully applied for the determination of nitacrithiazole in pharmaceutical formulations and urine samples, gives a good standard deviation values and time consume less and inexpensive. The analytical performances obtained in the present work for this substance are very better than previous methods.

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