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Electroanalytical determination of Azapropazone at Glassy Electrode Using Differential Pulse and Anodic Square-Wave Voltammetry in Pure Formulation and Pharmaceutical Formula

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Abstract
A sensitive electroanalytical method for determination of azapropazone has been investigated on the basis of the enhancement electrochemical response at glassy carbon electrode during oxidation of azapropazone, Cyclic voltammetric undergo one irreversible anodic peak at Ep = 0.48 mV in Britton - Robinson (BR) (pH 4.0). Cyclic voltammetric study indicated that the oxidation process is irreversible and adsorption controlled. The number of exchanged electrons in the electro -oxidation process was obtained. Differential pulse voltammetry (DPV) and square wave voltammetry (SWV) were studied and a linear calibration obtained from: 0.0014–0.026µg/ml, 0.014–0.134µg/ml using DPV and SWV respectively. The RSD for five measurements were found in the ranges: 0.854% and 0.911% for DPV and SWV, respectively. Precision and accuracy of the developed method was checked by recovery studies. The method was applied to determine azapropazone in pure form, pharmaceutical formulations, and compared with official methods.

Key Words: Azapropazone, Voltammetry; Differential pulse, cyclic voltammetry and square wave voltammetry.

Introduction

Azapropazone (RS)-5-dimethylamino-9-methyl-2-prop-2-enylpyrazolo [1, 2-a] [1, 2,4] benzotriazine-1,3-dione is a non-steroidal anti-inflammatory drug. It is manufactured by Gold shield under the tradename Rheumox [(1)]. It was available in the UK as a prescription-only drug, with restrictions due to certain contra-indications and side effects[(2)]. AZA has now been discontinued in the BNF 60 (British National Formulary). Molecular structure of azapropazone is given in Fig (1). Different methods have been reported for the determination of AZA drug, including thin-layer chromatography[(3)], high performance liquid chromatographic method (HPLC)[(4-10)] However, most of these methods are complicated or not available whereas but electrochemical methods have proved to be very sensitive for the determination of organic molecules, including drugs and related molecules in pharmaceutical dosage forms and their oxidize able property. Carbon electrodes, especially glassy carbon electrode is widely used in the electrochemical investigations because of their low background current, wide potential windows, chemical inertness, low cost, and suitability for detection of various organic and biological compounds. Among these glassy carbon electrode (GCEs), due to unique characteristics such as versatility of chemical modification, have been extensively used.

In this work, we report our recent research into the electrochemical properties and oxidation behaviour of AZA drug at glassy carbon electrode. The electrode process dynamics parameters were investigated by using several electrochemical techniques cyclic voltammetry (CV), deferential pulse (DPV) and square wave voltammetry (SWV). Simultaneously, a high sensitivity electro analytical method is established.

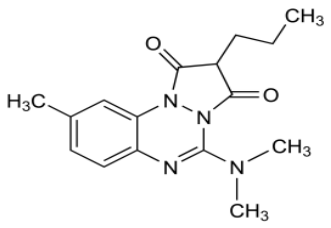

Fig (1): Molecular structure of azapropazone

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Experimental

Apparatus

All voltammetric experiments were carried out using a Metrohm computrace voltammetric analyzer model 797 VA with Software Version 1.0 (Metrohm Switzerland. With a three-electrode conFiguration: glassy carbon disc electrode as working electrode (mini glassy carbon disk electrode of the active zone: 2.8mm, for ELCD 641/656), Ag/AgCl (3M KCl) as reference electrode and a platinum wire counter electrode were used. A digital pH/mV meter (JEANWAY 3510) with a glass combination electrode was used for the preparation of the buffer solution. A micropipette (Eppendorf-multipette plus) was used throughout the present experimental work.

Reagents

Azapropazone was supplied from Delta pharm Pharmaceutical Co, 10th of Ramadan city, Area B4 Egypt. The purity of the sample was found to be 99.8% on the dried basis. Stock solutions of 10^{-3} M was prepared by dissolving an appropriate weighed of AZA in 25 ml methanol then complete to 100 ml in measuring flask with the bidistilled water to give 1x10-3M. . The stock solution was stored in a refrigerator for one week. Britton - Robinson (BR) buffer solutions (2.0-12)[11] were used as supporting electrolyte. All solutions were prepared by using analytical grade reagents in bidistilled water.

Working electrodes

To improve the sensitivity[12] and resolution of the voltammetric peaks, the glassy carbon electrode (GCE) was polished manually with 0.5 µm alumina powder on a smooth polishing cloth prior to each electrochemical measurement. Then, it was thoroughly rinsed with methanol and double distilled water, and gently dried with a tissue paper.

Preparation of tablet sample assay

Ten tablets of AZA were crushed into a fine powdered in a mortar. A 300 mg of this powder was accurately weighed and then dissolved in 25 ml methanol. It was sonicated for 5 minutes. The content was allowed to settle after stirring magnetically for 5.0 min. The sample solution was filtered through a whatman no. 42 Filter paper. Aliquot of the solution containing the nominated range concentration of AZA was added into a 50 mL measuring flask and the procedure completed as described above.

The optimizations

To obtain the optimum pH, an appropriate amount of AZA working standard solution of 10^{-3} M was placed in the electrolytic cell, which contained 25 ml of BR buffer solution and the cyclic voltammogram was recorded. The experiment was repeated by using buffer solutions of different pH values (2.0-12) and the optimum pH was obtained.

The effect of scan rate (υ) on the peak current (Ip) of AZA was studied, the working electrode was immersed in the optimum buffer solution containing an appropriate amount of AZA standard solution $1.0x10^{-6}$M, and the cyclic voltammograms were recorded at different scan rates over the scan range 10-250 mV/s. Plot log Ip versus log υ to know the nature of the process, diffusion controlled process or adsorption controlled process.

To study the effect of accumulation time, the working electrode was immersed in the optimum buffer solution containing an appropriate amount of AZA standard solution 1.0 x 10^{-6} M to select times with stirring at 1200 rpm at open circuit condition. After accumulation, the cyclic voltammograms were recorded then plot the peak current (Ip) versus time to obtain the optimum accumulation time.

The optimum instrumental conditions for the determination of AZA by using DPV and SWV methods were chosen from a study of the variation of the peak current with pulse amplitude (pulse width and scan rate). During the study, each parameter was changed while the others were kept constant: pulse amplitude over the range of 30-100 mV, pulse width 30-80 ms, and scan rate 20-250mV/s.

General procedure

Supporting electrolyte BR buffer of pH 4.0 (25 ml) was placed in the voltammetric cell and the required volume of standard AZA solution was added by micropipette. The solution was continuously stirred at 1200 rpm when accumulation potential (usually open circuit conditions) was applied for a certain time to the working electrode. At the end of accumulation period, the stirring was stopped, and after 5.0 sec rest period was allowed for the solution to become quiescent. The used drug was determined by using DPV and SWV methods. Aliquots of the drug solution of 10^{-3} M were introduced into the electrolytic cell and the procedure was repeated. The voltammograms were recorded. The peak current was evaluated as the difference between each voltammogram and the background electrolyte voltammogram. All measurements were carried out at room temperature.

Results and discussion

Electrochemical behavior of azapropazone at GCE

To understand the voltammetric process occurring and reversible behavior of AZA redox reactions on the glassy carbon electrode cyclic voltammetry was carried out. Another two different techniques were developed for the quantitative determination of AZA based on DPV and SWV methods. Fig. 2

shows the continuous cyclic voltammograms of 1.0 x 10^{-6} M AZA on the GCE electrode at scan rate 100 mV/s in pH 4 BR buffer. During the first cycle appears to be an electro active drug. It was oxidized on glassy carbon electrode between 0 □1.0V, producing one well-defined sensitive oxidation peak irreversible oxidation peak appears at 0.48 V on the anodic sweep. In the successive cycles, without the reduction peak, indicating an irreversible electrochemical process.

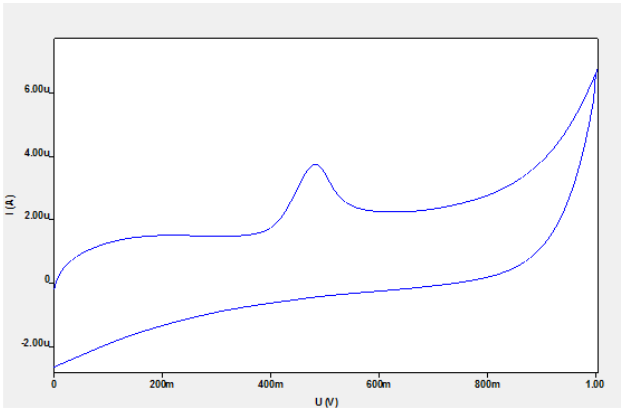

Fig. 2. Cyclic voltammetric response of 1.0 x 10-6 M AZA at GCE electrode in pH 4 BP buffer. Scan rate is 100 mV/s.

Effect of pH

The effect of solution pH on the electro oxidation was studied by cyclic voltammograms using Britton–Robinson buffers within the PH range of 2–10. It was found that electrochemical behavior of AZA is dependent on the pH value of the aqueous solution and the pH of the solution has a significant influence on the peak current and potential of the oxidation of AZA, Fig.3. Shows the plot of peak current (Ip) vs. pH indicating that the peak current reaches its maximum value at pH 4 glassy carbon electrode Therefore, this pH was selected as the optimal pH.

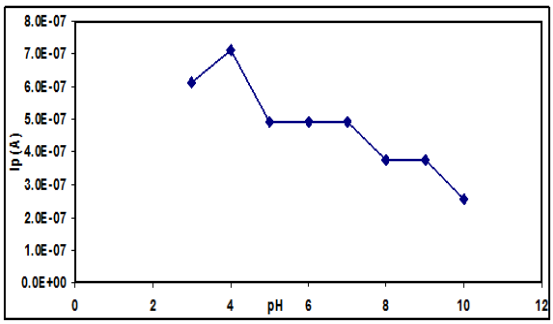

Fig.3. Effect of pH on peak current of 1.0 x 10-6 MAZA solution in BR buffer at CPE paste and GCE at a scan rate 100 mV/s

The anodic peak potentials shifted negatively with the increase of the solution pH, indicating that the electro oxidation is a pH- dependent reaction and that protons have taken part in their electrode reaction processes. Also, the peak potential for AZA oxidation varies linearly with pH (over the pH range from 2 to 10). The dependence of Ep on pH can be expressed by the relation:

E pa (V) = 0.4772 □□ 0.053 pH having correlation coefficient of 0.995

The slope of −56.14 mV/pH indicated that the equal numbers of proton and electron involved in the process of electrochemical oxidation of AZA [13]. For an exact Nernstian response, the slope would be expected to be 0.061 for one-electron and one-proton process [14, 15].

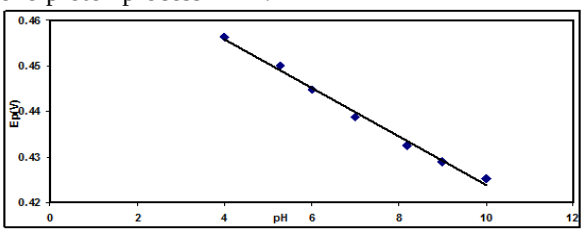

Fig. 4. Variation of anodic peak potential of 1.0 x 10^{-6} M AZA solution in the pH 4.0 of buffer solution at the glassy carbon electrode in the sweep rate of 10 mV/s.

Effect of scan rate

The effect of the potential scan rate on the peak current (Ip) for (1 x 10^{-6} M) AZA solution was evaluated over the scan range 20-300mV/s as shown in Fig.5. The variation of the peak current (Ip) with the voltage scan rate (υ) for the irreversible electrode reaction was given by the relation[11].

Ip = 2.69×10^5 n3/2A D1/2Cυ1/2 at 298K°

Where, Ip = current (A), n = number of electrons, F = Faraday constant, 96,485 C/mol, A = area of the electrode cm^2, C = concentration (mol/cm3), D = diffusion coefficient (cm^2/s), υ = scan rate (V/s)

So the data is plotted as log-log graph. This confirming the irreversibility of the electrochemical processes with simultaneous increase in the peak current at high scan rate. A good linearity between log Ip and the log scan rate υ were obtained from the range of 20 ~ 300 mV/s shown in Fig (6). The plot of log Ip as a function of log υ give linear increase in the oxidation peak current with the scan rate which displayed a linear correlation and give the regression equation as follows: log Ip = 5.2898+ 0.482 log υ.

The slope values obtained are close to the theoretical value (0.5) which demonstrated that the electrode reaction is ideal reaction of the solution species. Thus the oxidation is diffusion[16, 17] controlled process over the studied scan rates at GCE electrodes. This evidence can enhanced by observing that, the accumulation time had no effect on the anodic peak current.

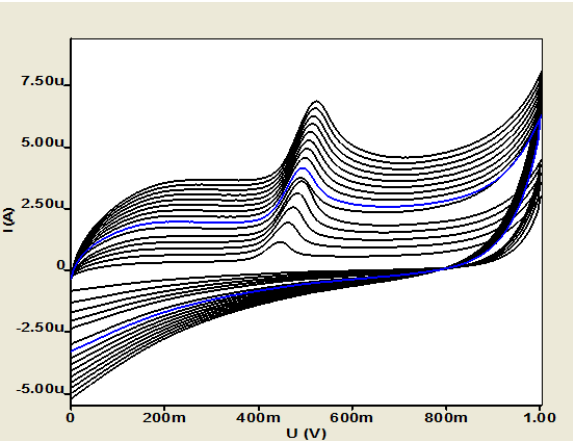

Fig.5. cyclic voltammetry of 1x 10-6 M AZA solution in BR buffer of pH 4.0 at different Scan rate (20- 300 mv/sec) at GCE.

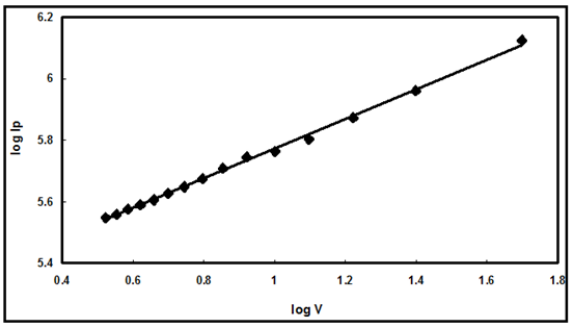

Fig. 6. Effect of scan rate (υ) on Anodic peak current of 1x 10-6 M AZA solution in BR buffer of pH 4 at GCE.

Determination of AZA in the pure form

AZA was electro oxidize glassy carbon electrode in the working potential range 0–1000mV. However, AZA showed a well oxidation 426, 525mV potential at glassy carbon electrode by differential pulse (DVP) and square wave voltammetry (SWV) as in Fig (7, 8). The plot of peak current of the oxidation peak with concentration illustrated in Fig (9,10) showed that the peak current of the oxidation peak increased with increasing in concentration of AZA. Analytical method was developed involving differential pulse (DVP) and square wave voltammetry (SWV) for the determination of the drug under investigation. The peak current shows a linear dependence with AZA concentration between 0.0014–0.026µg/ml, 0.014 – 0.134 µg/ml at glassy carbon electrode, using DVP and SWV respectively. The calibration plots were described by the following equations:

Ip (µA) = 6E-09 C (µM) + E-07 (Correlation coefficient) = 0.9956 for DVP

Ip(µA)=1E-08 C (µM) + 2E-07 (Correlation coefficient)=0.9911 for SWV.

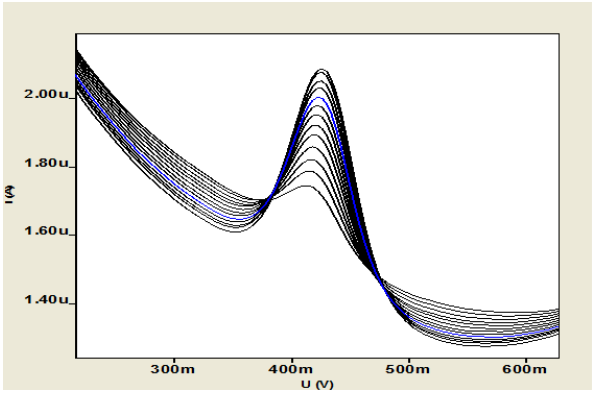

Fig. 7. DVP voltammograms recorded for AZA at GCE.

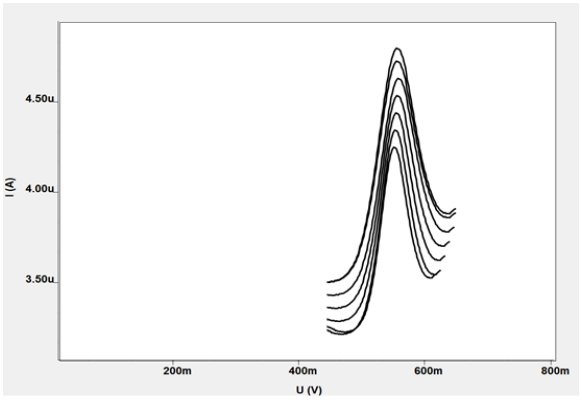

Fig. 8. SWV voltammograms recorded for AZA drug at GCE.

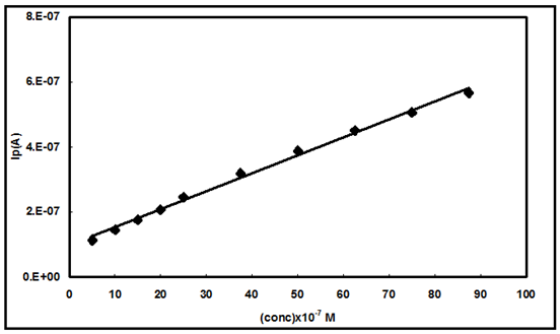

Fig. 9. Calibration curves of AZA at GCE by using DPV method, pulse amplitude 50 mV at scan rate of 20 mV/s.

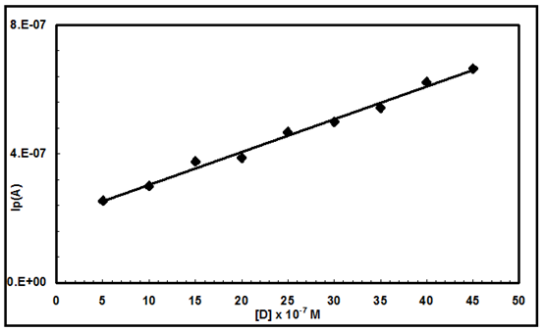

Fig. 10. Calibration curves of AZA drug at GCE electrode using SWV method, 50 mV, pulse amplitude 19.99 mV and scan rate 19.84 mVs-1

Analytical applications of commercial tablets

The applicability of the proposed method for determination of AZA in pharmaceutical form containing tablets were examined for estimating AZA content present in commercial dosages. DVP and SWV were recorded under exactly identical a condition that was employed while recording for plotting calibration plot. The proposed method was successfully applied to the direct determination of Prolixan without interference from common excipients used in pharmaceutical preparations. The linearity range was 0.0016– 0.024µg/ml, with mean relative standard deviation of 0.854 %.in case DPV. The linearity range was 0.02–0.15 µg/ml with mean relative standard deviation of 0.911 % in case SWV For glassy carbon electrode as shown in Table (1s). According to the Student's t-test, Statistical analysis of the results showed no significant difference between the performance of the official and proposed methods as regards to accuracy and precision.

Table (1): Evaluation of the accuracy and precision of the proposed and official methods for the determination of AZA. In it's pharmaceutical forms at GCE

Prolixan	[Drug]	Proposed method ±%RSD, n=5	Official method ±%RSD, n=5	F-test	T-test
DVP	300mg	100.16 ± 0.3	100.21± 2.2	1.2	2.13
	600mg	99.92 ± 1.01	99.62 ± 0.87	1.32	2.22
SWV	300mg	100.11 ± 0.2	100.10± 1.1	1.82	2.11
	600mg	99.97 ± 1.04	99.72 ± 0.76	1.56	2.03

Conclusions

The statistical calculations for the assay results show good precision of the voltammetric method. According to the t-test, there was no significant difference between the calculated and comparative values at the 95% confidence level with an acceptable range of error, indicating that the DVP and SWV can be used for voltammetric determinations of AZA drug in pure form and pharmaceutical forms. It is simple, low cost, sensitive, selective, accurate and precise. The sensitively and selectivity of the procedure could be improved by the preconcentration of the drug from large sample volumes under the optimum experimental condition. The method developed also showed good ability to quantify drug contents in tablets with reliable accuracy.

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