ORIGINAL RESEARCH ARTICLE

VOLTAMMETRIC DETERMINATION OF PIOGLITAZONE IN PHARMACEUTICAL AND HUMAN URINE SAMPLES USING CARBON PASTE ELECTRODE

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Abstract: The electrochemical behaviour of Pioglitazone (PGZ) drug was studied using carbon paste electrode (CPE) in Britton Robinson (BR) buffer solution. Here Cyclic voltammetry and differential pulse voltammetric techniques were employed for this determination. The reduction process was shown to be irreversible over the pH range (2.0–10.0) and the well-defined reduction peaks are obtained at -1.80V based on diffusion controlled. Effects of cathodic peak potential, current (I_{pa}), scan rate, pH, etc., have been discussed. A possible electro reduction mechanism was proposed. An analytical method was developed for the determination of pioglitazone in BR buffer solution at pH 6.0 as a supporting electrolyte. The cathodic peak current varied linearly with pioglitazone concentration in the range 6.25×10^{-5} M to 3.25×10^{-3} M with a limit of detection (LOD) of 2.65×10^{-10} M and limit of quantification (LOQ) of 4.52×10^{-8} M. The proposed method was successfully applied to the determination of pioglitazone in pharmaceutical and human urine samples.

Key words: Pioglitazone; carbon paste electrode; cyclic voltammetry and differential pulse voltammetry; LOD

INTRODUCTION

Pioglitazone (PGZ) is a thiazolidine dione antidiabetic agent, chemically it is (Rs)-5-(4_[2-5-ethylphyridin-2-yl) ethoxy] benzyl) thiazolidine - 2,4-dione. Pioglitazone modulates the transcription of the insulin sensitive genes involved in the control of glucose and lipid metabolism in the muscle, adipose tissue and in the liver. It is used in the treatment of type-1 diabetes mellitus. Pioglitazone targets insulin resistance and, hence, is used alone or in combination with insulin, metformin, or a sulfonyl urea as an antidiabetic agent [1]. PGZ decreases the plasma glucose concentrations insulin concentrations, and glycosylated hemoglobin. Additional favorable metabolic effects include decreased hepatic glucose output, lower free fatty acid concentrations, and improved lipid profiles. Thiazolidine diones such as pioglifazone help insulin to work more effectively [2].

Several spectrophotometric methods have been reported for the estimation of PGZ including ion-pair complex formation with bromothymol blue, bormo phenol blue and bromocresol purple and chlorophenol red as well as interaction with diazotized sulfanilic acid Chromatographic methods have been reported such as very rapid separation and quantification of PGZ HCl in the presence of metformin HCL on monolithic column as well as a stability indicating densitometric RP-TLC method [3-8]. Flow injection analysis, voltammetry, derivative spectrophotometry and capillary electrophoresis methods have been reported [9-14].

Carbon paste electrodes (CPEs) represent one of the most frequent types of working electrodes. A simple method of direct mixing of a solid modifier to the paste which was the commencement of explosive research activity in this field. Quite a few reviews are exclusively devoted to CPEs [15-21]. Carbon paste electrodes (CPEs) belong to promising electrochemical or bioelectrochemical sensors of wide applicability. The base of modified carbon pastes is usually a mixture of powdered graphite and nonelectrolytic binder.
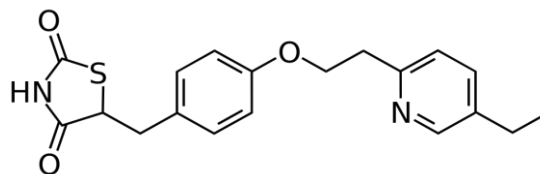

Figure 1: Structure of pioglitazone

However most of these methods are time consuming therefore, focus of the present study was to develop an accurate, precise and robust voltammetric method for the determination of pioglitazone hydrochloride in pharmaceutical and urine samples. In the present work focused on an electrochemical analysis of PGZ in human urine samples with CPE. Therefore, a rapid and sensitive voltammetric method has been applied for the determination of PGZ in pharmaceutical and human urine samples.

MATERIALS AND METHODS

The voltammetry experiments performed with auto Lab PG STAT 101 supplied by Metrohm Autolab B.V., The Netherlands. A Three electrode system comprising of a Carbon paste electrode (CPE) as a working electrode, a saturated Ag/Agcl/Kcl as a reference electrode and Pt wire as a counter electrode

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obtained from local scientific labs. An Elico LI-120 P^H meter supplied by Elico LTD, Hyderabad, India was used to determine the p^H of the buffer solution. All the solutions examined were carried out at room temperature 25±2°C.

Reagents and solutions

Solutions were prepared in double distilled water pioglitazone Hydochloride active pharmaceutical ingredient were supplied by Hetero pharma, Hyderabad. A standard stock solution was prepared by dissolving an accurately weighed amount pioglitazone Hydrochloride drug in DMSO. The solution was stored under room temperature. More dilute solutions of the drug were prepared in volummetric flask by diluting the stock solution with buffer to get desired concentration. The Britton-Robinson buffer was prepared by using 0.2 M boric acid, 0.05M citric acid and 0.1M trisodium orthophosphate and pH were adjusted by 0.2 mol L^{-1} NaOH for the use of supporting electrolytes. Desired concentration of solution was prepared from stock solution.

Preparation of working electrode

The carbon paste was prepared by thoroughly mixing 5 gm of graphite powder with 1.8 ml of paraffin oil in a mortar with pestle. The carbon paste was packed into the hole of the electrode body and smoothed on a clean paper until it had a shiny appearance. The electrode body was constructed by pressing a small rode of stainless steel (diameter 3mm) inside a micropipette tip (1 ml volume capacity) leaving a depression at the surface tip approximately 1mm for housing the carbon paste, and a thin wire was inserted through the opposite end to establish electrical contact. The carbon paste electrode was immersed in the supporting electrolyte placed in the cell and several sweeps were applied to obtain a low background current.

Recommended procedure for the analysis

An accurate volume (10mL) of the BR buffer at the required pH was transferred to the electrochemical cell and the electrodes were immersed in test solutions through which a stream of nitrogen is purged for 15 min before recording the voltammograms. The scans were initiated in the negative direction of the applied potential from +0.V to -2.0 V. After recording the voltammogram of the blank solution, an accurate volume (0.505.0ML) of the drug solution was added. The cathodic potential sweep was then recorded under different operating conditions of pH, sweep rate. And pulse amplitude. The effect of scan rate on the voltammograms was determined using the same solution.

RESULTS AND DISCUSSION

Cyclic voltammetric (CV) behaviour of PGZ

A single, fine clear reduction peak was obtained for PGZ (6.25x10^{-5} molL^{-1}) involving four electrons four proton reduction of the carbonyl group. In the reverse scan, on anodic peak was observed indicating the irreversibility of the reduction reaction (Fig.2) Using carbon paste electrode (CPE) at different pH values, the CV scan generated relatively low peak currents at higher cathodic potentials of -1.80 V vs. Ag/AgCl. Catalytic activity of CPE was demonstrated cyclic voltammetry. The increase in the peak current response and decrease in reduction potential demonstrates the synergistic effect on the electron transfer rate due to enhanced surface area of the electrode and the catalytic activity of the carbon paste electrode. Possible reduction mechanism of PGZ was shown in scheme 1.
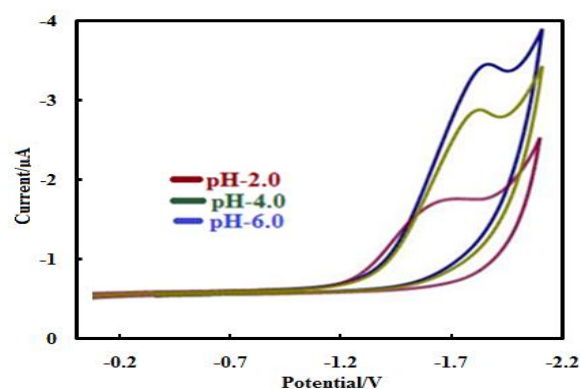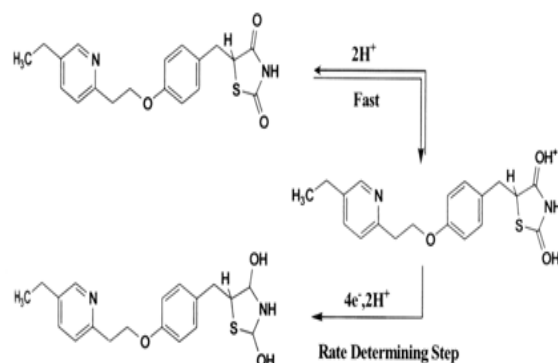

Figure 2: Typical cyclic Voltammograms of PGZ (6.25x10^{-5}M) at different pH values on CPE with scan rate of 0.1V/s.

Scheme 1: Electrochemical reduction mechanism of pioglitazone

Effect of accumulation conditions and pH

The accessibility of the protons is significant parameter in the electrochemical reduction studies. The peak current decreased when the change in pH was from 2.0 to 10.0, a well-defined reduction peek was observed at pH 6.0, and hence, pH 6.0 was selected as optimum pH based on sharp, reproducible peak signal. As pH increases, peak potential shifted to negative

values indicting proton participation in the electrochemical reduction of PGZ. A plot of Ep vs. pH gives a slope of 32m V/pH indicating proton electron equivalence (Fig.3). Further maximum peak signals of PGZ were observed with the electrode at an accumulation potential of -1.80 V and accumulation time of 100 sec.
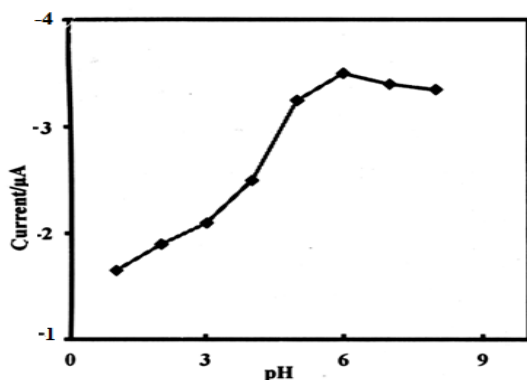

Figure 3: The plot the of current vs pH of PGZ in BR buffer solution, concentration: 6.25×10^{-5}M at CPE in different pH values from pH 2.0 to pH 10.0.

Effect of scan rate

The effect of scan rate (V) on the peak current and peak potential of PGZ at carbon paste electrode shown in Fig.4. The influence of the square root of the scan rate on the peak current showed a linear relationship between −25 to -100 mVs-1, which is of typical diffusion controlled process. The slope of the theoretical value and expected value is close to each other. This indicates that the electrode process was controlled by diffusion controlled process. The peaks are shifted to negative values with increasing the scan rates.
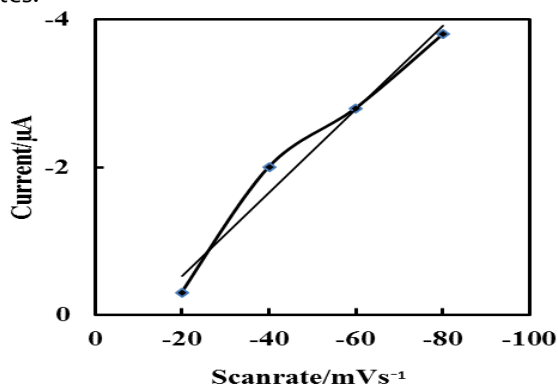

Figure 4: Linear plot of current Vs scan rate for 6.25×10^{-5}M of PGZ at CPE in BR buffer of pH 6.0

Differential pulse voltammetric (DPV) determination of PGZ

A working standard of PGZ (6.25×10^{-5} molL^{-1}) was prepared for the standard solution using double distilled water. 10mL of test solution consists of 1.0 mL of the working standard and 9.0 mL of the BR buffer of

pH 6.0 was taken into the electrolytic cell and the solution was purged with nitrogen gas for 15 minutes. The potential of the working electrode was scanned from 0 to -100 mV/s vs. Ag / AgCl. The compound gave single, well defined peak signal at -1.80V. DPV signals for PGZ at CPE for a series of concentrations 6.25×10^{-5} molL^{-1} to 3.25×10^{-3} molL^{-1} were recorded under identical conditions (Fig.5). Enhanced peak current responses and reduced peak potentials were observed for the studied compound at CPE, the increased electrical conductivity and fast electron transfer rate of CPE.
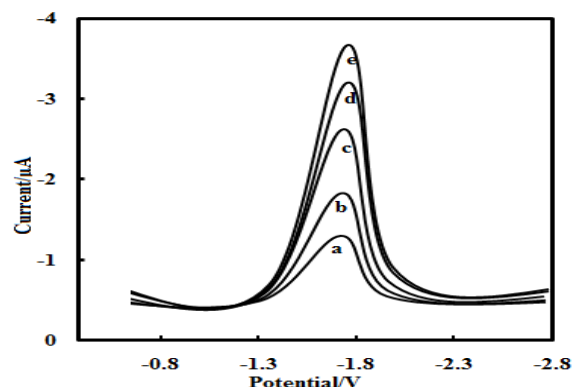

Figure 5: DPV curves using CPE for PGZ at concentrations, 3.25×10^{-3}M to 6.25×10^{-5}M

Calibration plot

A calibration plot was drawn between the concentration and peak current of PGZ over the range 1×10^{-3} molL^{-1} to 1×10^{-5} molL-1. It was shows that the peak current increases linearly with the concentration of PGZ. The linear regression equation as given by: Y= -0.489x+0.4776 with a correlation coefficient of 0.9989. The limits of detection (LOD = 3s/m) and limits of quantization (LOQ = 10s/m were calculated as 2.65×10^{-9} molL^{-1} and 3.72×10^{-7} molL-1. Where's' is the standard deviation of the intercept and 'm' is the slope of the calibration curve and also recovery study of PGZ.

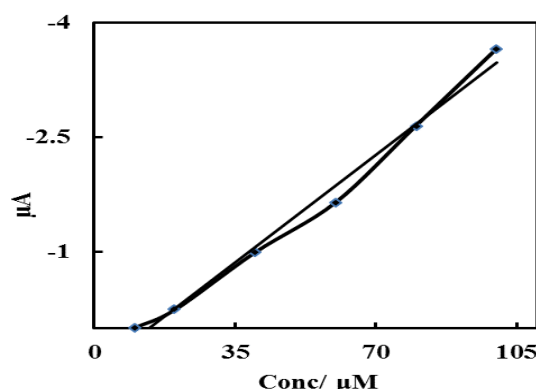**Figure 6:** Calibration plot of the PGZ in BR solution of pH6 at different concentrations from 3.25×10^{-3}M to 6.25×10^{-5}M at CPE, scan rate 100 mV/s

Table 1: Determination of PGZ in Pharmaceutical samples and Urine samples

Pharmaceuticals					
Sample		Labelled amount (mg)	Amount found (mg)	Recovery %	RSD %
Pioglit	1	5	4.86	97.20	1.85
	2	10	9.68	96.80	2.35
	3	15	14.46	96.48	2.76
Urine samples					
Pioglit	1	5	4.97	99.58	1.54
	2	10	9.89	96.18	1.69
	3	15	14.80	98.66	2.45

CONCLUSION

The electrochemical determination of PGZ in pharmaceutical and human urine samples at carbon paste electrode was examined in BR buffer over the pH range from 2.0 to 8.0 by differential pulse voltammetry. The drug exhibits lower current and negative potentials with lower detection limit of 6.25×10^{-9} molL^{-1}. The simple, sensitive, selective, fast and low cost voltammetric method was developed for the determination of PGZ in pharmaceutical formulation and spiked serum samples.

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