

Voltammetric Determination of Esomeprazole using Carbon Paste Electrode Modified by Nanoparticles Oxide, and its Application on Tablet and Serum

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Abstract:- The anodic voltammetric behavior of esomeprazole (ESO) was explored at carbon paste electrode modified by mixture of CuO/ZnO nanoparticles (CPE/ CuO ZnO NPs) in B.R buffer (PB) solutions over the pH range (2.0-11.0) using cyclic and linear-sweep voltammetry (CV; LSV). The oxidation of ESO was shown to be irreversible and diffusion-adsorption controlled driven process. Under optimized conditions, the LSV peak currents were in a linear relationship to ESO concentrations in the range of (1x10⁻⁷ M– 1x10⁻⁶ M) with a detection limit of 3.1 x10⁻⁸M. The LSV was successfully employed for the determination of ESO in tablet. The voltammetric procedure was successfully also applied for rapid analysis of ESO in stability studies without interference from the degradation products.

Keywords: Esomeprazole , Voltammetry Carbon Paste electrode, Stability, Nanoparticles pharmaceutical analysis, Cyclic Voltammetry

1. INTRODUCTION

Esomeprazole (S)-(c)-5-Methoxy-2-[(4-methoxy- 3,5-dimethylpyridin-2-yl)methylsulfinyl]-3H-benzoimidazole (ESO), is a PPI developed as an optical isomer, the S isomer of OMZ, with the aim of improving the pharmacokinetic and pharmacodynamic profiles of racemic OMZ [1-4]. This optical isomer is subject to less first-pass metabolism and lower plasma clearance than OMZ, thereby offering higher systemic bioavailability [5]. ESO has higher and more consistent bioavailability than OMZ. It suppresses the secretion of hydrochloric acid from gastric parietal cells via inhibition of the H⁺/K⁺ adenosine triphosphatase enzyme, similar to other PPIs [6]. It is used in the treatment of dyspepsia, peptic ulcer disease, gastroesophageal reflux disease, and Zollinger-Ellison syndrome [7]. ESO is effective and well-tolerated in the maintenance of healing of erosive oesophagitis and demonstrates significantly greater efficacy than omeprazole in the treatment of GERD patients with erosive esophagitis [8]. On the other side, unlike OMZ, ESO-based triple therapy can effectively eradicate Helicobacter pylori (Hp) infection and heal patients with duodenal ulcer (DU) without the need of follow-up monotherapy [9].

Up to now, few works about esomeprazole analysis have been reported. Spectrophotometric methods have been reported for determination of ESO in its magnesium trihydrate salt or tablet dosage form [10-12]. Chromatographic methods for the determination of ESO in tablets [13]. Recently, electroanalytical techniques have been widely used for the determination of pharmaceuticals compounds [14-19]. The electrochemical methods in general have many advantages including the ease of operation, fastness, simplicity, sensitivity, energy saving, low cost and reliability of the electrochemical techniques [20-24]. Although some efforts have been made to detect ESO in the field of analytical chemistry, it is still a challenge to develop some new materials to further achieve sensitive and facile detection.

The nanoparticles in particular exhibit unique properties that make it possible to be used in a variety of applications, [25-28]. The results obtained demonstrate that the developed electrode has multiple virtues such as simplicity, flexibility and cost-effectiveness.

2. EXPERIMENTAL

2.1 Materials

ESO standard was procured from Sigma- Aldrich, Laboratories Co. Ltd. An aqueous stock solution of ESO (1×10⁻²M) was freshly prepared every time by dissolving accurately weighed amounts in double distilled water. The required concentrations of ESO in the supporting electrolyte were then prepared by dilution of the standard stock solution. BR buffer solution in the pH range 2.0 to 11.0 was prepared.

2.2 Instrumentation

A potentiostat model 263 (EG& G PARC) Princeton applied corporation (made in the USA) The potentiostat accomplished with a three-electrode system, the working electrode (WE) is carbon paste electrode modified by mixed nanoparticles, the Ag/ AgCl used as reference electrode while a Pt wire was used as the counter electrode.

2.3 Preparation of working electrodes

The modified working electrode was prepared in this study, by mixing 60% graphite powder and 25% with paraffin wax and 15% nanoparticles. The mixture heated till melting. The resulted paste was then packed into the end of an insulin syringe. External electrical contact was established by forcing a copper wire down the syringe.

3.1. CYCLIC VOLTAMMETRIC BEHAVIOR OF ESO

The recorded CV voltammograms indicated that, the studied compound undergoes oxidation process. **Fig.(1)** represents the oxidation process of 1×10^{-5} M in B.R buffer, pH=7.00 at a scan rate 50 mV/s on the surface of CPE modified by mixed nanoparticles. The anodic peak was observed at 1.0V. During the reverse scan no reduction peak was observed

3.2. EFFECT OF SUPPORTING ELECTROLYTE

The effect of supporting electrolyte were examined on the oxidation peak of ESO at the same conditions such as sodium phosphate, sodium nitrate, Britton-Robison buffer, sodium sulfate, sodium chloride, potassium chloride, sodium acetate buffer and borate buffer. Britton-Robison buffer, phosphate buffer, acetate buffer have a response toward electro-oxidation peak of ESO. The shape and the height of the oxidation peak of ESO were taken into consideration on choosing the suitable supporting electrolyte. The results showed that the suitable oxidation peak (shape and height) of ESO in Britton-Robison buffer. The shape and the height of the oxidation peak of ESO were taken into consideration on choosing the suitable supporting electrolyte. The results showed that the suitable oxidation peak (shape and height) of ESO in BR buffer **Fig. (2)** Illustrated the voltammograms of 4×10^{-5} M of ESO on CPE modified by mixes nanoparticles in pH=6.0 in different kinds of supporting electrolytes.

3.3. EFFECT OF PH

The effect of pH value consider an important factor affecting the electro oxidation of ESO compound in aqueous solution. The pH values of B.R buffer was examined over the rang (pH=5.0 – pH= 9) on the oxidation peak of 1×10^{-5} M ESO as shown in **Fig (3A)**. The results showed that ESO degrades in acidic solutions unless it may be protected against acid conditions, so a significant decomposition is observed in solutions with pH values below 5.0 with a color change of solution, so we studied solutions with pH values equal or more than 5.0. The results showed that the potential of anodic peak of ESO is shifted again linearly towards negative values by increasing in the pH since the reaction of ESO at the surface of the electrode is more favorable. The best pH value was chosen is pH=7. The plot of E_p verses pH **Fig. (3B)** gave a linear relation and expressed in the following equation:

$$E_p \text{ (V)} = 1.36 - 0.074 \text{ pH} \quad r^2 = 0.865$$

With a slope of 0.074 (V/pH), this value suggests an equal number of electrons and protons in the ESO oxidation. These displacements are in accordance with the ones reported in the literature for ESO oxidation [29, 30].

3.4. EFFECT OF SCAN RATE

The electro oxidation peak of 1×10^{-5} M ESO in 0.1M B.R buffer (pH=7.0) using CPE modified by mixed nanoparticles was studied at different scan rates varying from 20 to 300mV/s, By increasing scan rate the oxidation peak current increased and shifted slightly to the positive side as shown in **Fig.(4A)**. But at scan rate more than 100mV/s the peak shape was distorted specially at high concentration of ESO so the scan rate of 50mV/s was selected for further work to avoid the distortion of the peak at higher concentrations of the ESO. The plots of peak currents against the square root of the scan rates exhibited linear relationship with correlation coefficients of 0.99. Showing that the electro catalytic oxidation of ESO was diffusion control [30]. As indicated in **Fig. (4B)**

3.5. EFFECT OF CONCENTRATIONS (CALIBRATION CURVE)

Effect of ESO concentration on the oxidation peak current was examined over the range (1×10^{-7} – 1×10^{-6} M) in 0.1M BR buffer (pH= 7.0), the peak current at a potential of +0.8V increased proportionally with the ESO concentration **Fig.(5)** to yield a highly linear calibration plot **Fig.(6)**:

$$I_p \text{ (} \mu\text{A} \text{)} = 0.316 + 0.58 \text{ C (} \mu\text{M} \text{)} \quad r^2 = 0.954 \text{ n=7}$$

The limit of detection (**LOD**) and limit of quantification (**LOQ**) were calculated using the following equations [31-33]:
LOD = 3 s/m, **LOQ** = 10 s/m

Where **s** is the standard deviation of the peak current (three runs) of the lowest concentration of the linearity range and **m** is the slope of the related calibration equation. **LOD** and **LOQ** were calculated as 3.1×10^{-8} M and 1.0×10^{-7} M, respectively.

3.6. REPRODUCIBILITY

The reproducibility of the results was examined by six successive measurements of 5×10^{-5} M ESO under the optimum experimental conditions. The relative standard deviation (RSD) was calculated and it was calculated to be 4.1 % indicating an acceptable reproducibility of the studied ESO at the modified electrode surface **Fig.(7)** illustrates six typical voltammograms for the repeated measurements of 5×10^{-5} M of ESO.

3.7 INTERFERENCES

In order to evaluate the selectivity of the proposed method, increasing concentrations of the possible interfering agents such as some metal ions, co-formulated substances such as glucose, starch, dextrose and sucrose and some organic acids were added to a solution with a fixed amount of ESO (1×10^{-6} M), and the corresponding voltammograms were recorded. The tolerance limit was defined as the maximum concentration of potential interfering substance that causes a relative error less than $\pm 5\%$ for determination of 1×10^{-6} M ESO. At about 100-fold excess, K^+ , Na^+ , Mg^{2+} , Ca^{2+} , Zn^{2+} , Cu^{2+} , Fe^{3+} , CO_3^{2-} , Cl^- did not significantly influence the height of the peak currents of (1×10^{-6} M) of ESO. In addition, effect of lactic acid, citric acid, oxalic acid, sucrose, dextrose, starch and glucose was studied and founded that at about 80 fold excess did not significantly influence the height of the peak currents of (1×10^{-6} M) of ESO. **Table 1** the proposed method was therefore found to be quite satisfactory for the selective determination of ESO by using CPE modified by mixed nanoparticles.

3.8 ANALYTICAL APPLICATIONS

The proposed method was applied to determine ESO in Pharmaceutical tablet and serum. Under the optimum conditions selected before, ESO has been determined. The concentration of ESO was determined using the method of standard additions and the recovery of the results ranged from 96% to 101.4%, and human serum with recovery ranged from 97.25% to 101.06%. with a good response as shown in **Table. 2**.

3.9. CONCLUSIONS

In this work a new handmade Nano modified carbon paste electrode with special properties such as catalysis, large specific surface area and more adsorption sites was succeeded in the determination ESO in tablet and serum under the optimum conditions as 0.1M B.R buffer (pH=7.00) and scan rate of 50mV/s. The suggested procedures can be used to detect the studied compounds with accurate, easily, rapidly, simple, cheap good reproducibility and low detection limit.

3.10. REFERENCES

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Tables

Table .1 Effect of some on the oxidation peak current of 1×10^{-6} M ESO.

Foreign species	Concentration (M) Upper limit	Signal change (%)
Na ⁺	1.0 x10 ⁻⁴	+1.2
K ⁺	1.0x10 ⁻⁴	-1.3
Zn ⁺²	1.0x10 ⁻⁴	-2.5
Cu ⁺²	1.0x10 ⁻⁴	-3.6
Mg ⁺²	1.0x10 ⁻⁴	-1.5
Ca ⁺²	1.0x10 ⁻⁴	-4.7
Fe ⁺³	1.0x10 ⁻⁴	+1.5
Co ₃ ²⁻	1.0x10 ⁻⁴	+1.15
Cl ⁻	1.0x10 ⁻⁴	-4.2
Lactic acid	8.0x10 ⁻⁵	-1.9
Citric acid	8.0x10 ⁻⁵	-4.1
Oxalic acid	8.0x10 ⁻⁵	-3.4
Glucose	8.0x10 ⁻⁵	-4.3
Dextrose	8.0x10 ⁻⁵	-2.5
Starch	8.0x10 ⁻⁵	-3.7
Sucrose	8.0x10 ⁻⁵	-1.3

Table .2 Recovery studies of Esomeprazole in pharmaceutical preparations.

Pharmaceutical Formulation	Standard added(mg)	Found (mg)	Recovery %
Esomeprazole ampoules	5	5.07	101.4
	10	9.96	99.6
	15	15.15	101
Biological fluid	Standard added x10 ⁻⁸ M	Found x10 ⁻⁸ M	Recovery %
Human serum	15	15.16	101.06
	30	29.5	98.3
	40	38.9	97.25

Figures

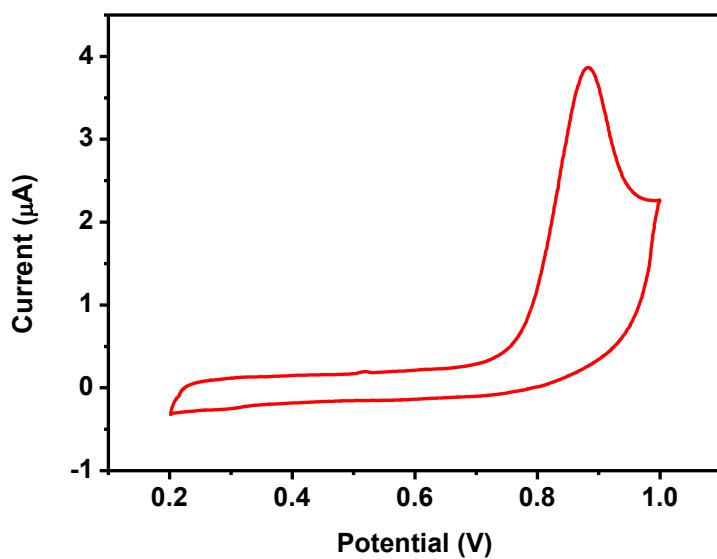


Fig. 1 Cyclic voltammograms of 1×10^{-5} M ESO at modified CPE in 0.1M BR buffer, pH=7.0 at a scan rate 50 mV/s.

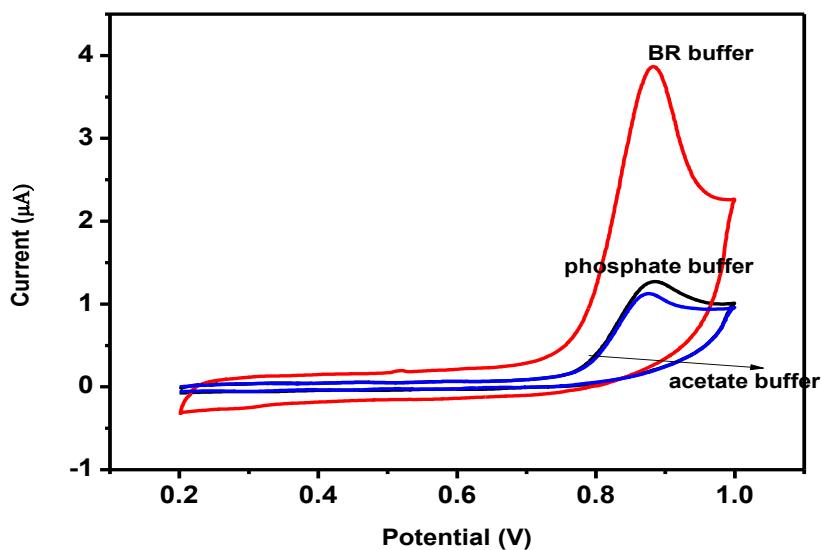


Fig. 2 Cyclic voltammograms of 1×10^{-5} M ESO at modified CPE in different supporting electrolytes and buffers, pH=7.0 at a scan rate 50 mV/s.

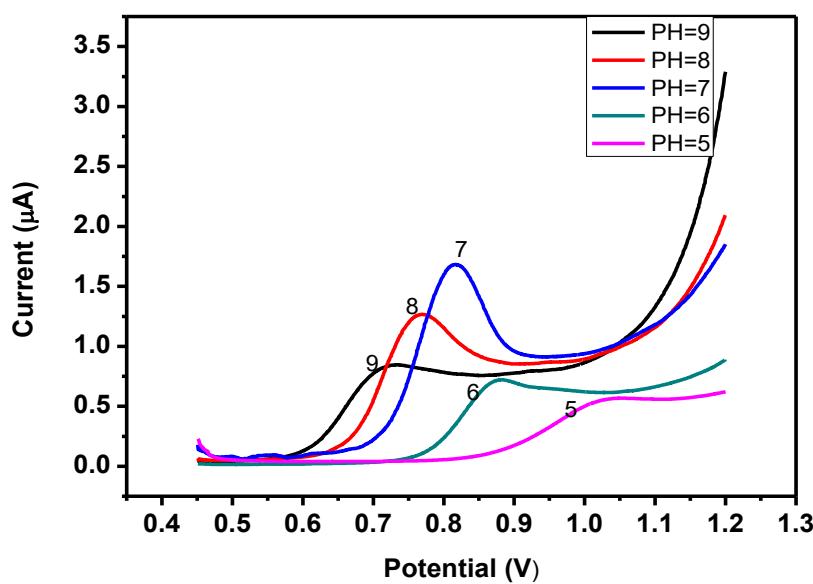


Fig. 3A Linear sweep voltammograms of 4×10^{-5} M ESO in (0.1 M) BR buffer at modified CPE scan rate 50 mV at different pH values.

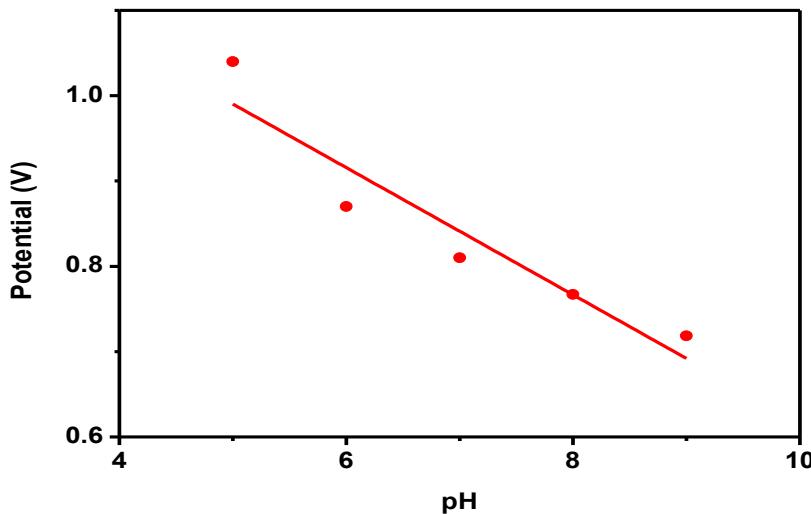


Fig. 3B Dependence of the peak potential of 4×10^{-5} M ESO on the pH of the supporting electrolyte.

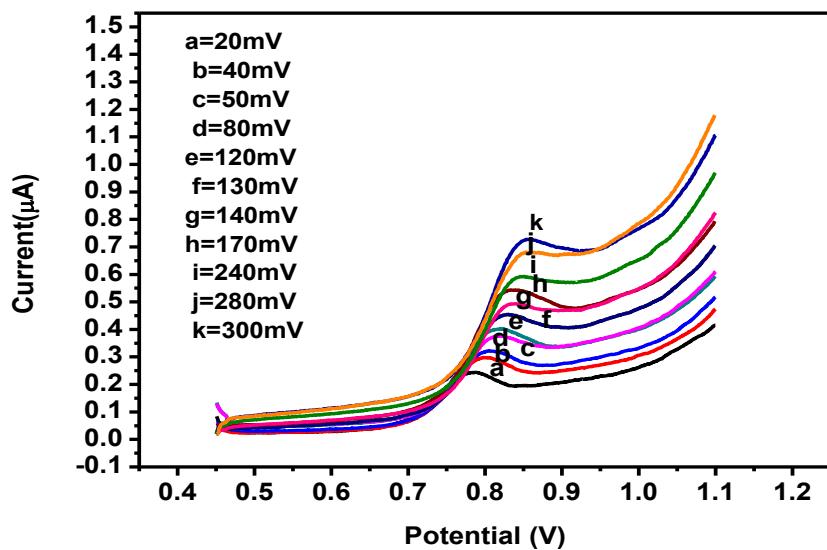


Fig. 4A Linear sweep voltammograms of 1×10^{-5} M ESO in (0.1 M) BR buffer (pH=7.0), on modified CPE at different scan rates.

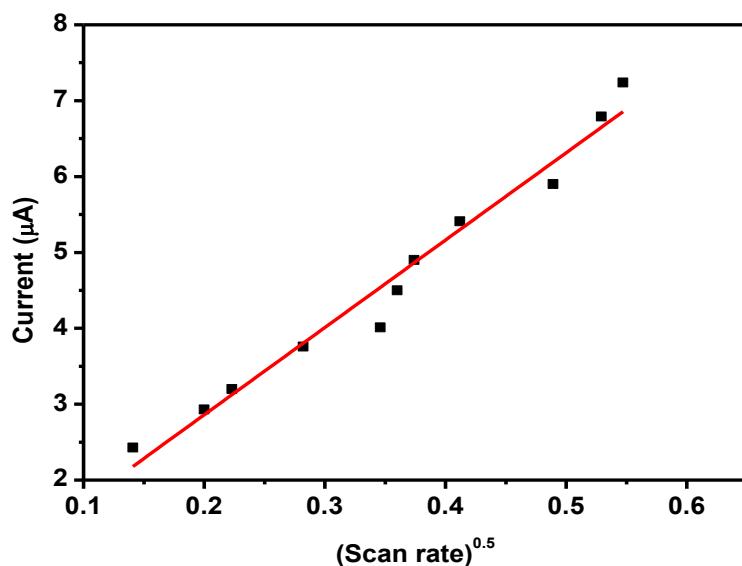


Fig. 4B The relation between the peak current of 4×10^{-5} M ESO in BR buffer (pH=7.0) using on modified CPE with the square root of scan rate.

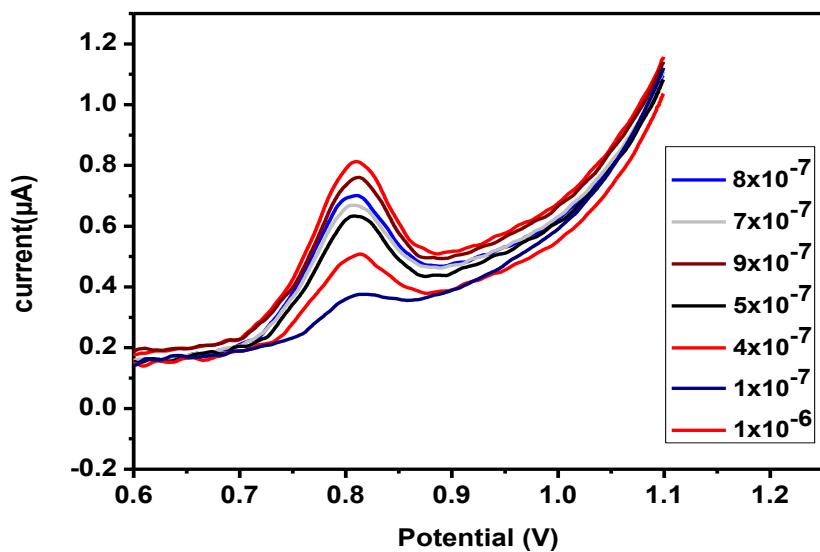


Fig.5 Linear sweep voltammograms for different concentrations of ESO in BR buffer (pH=7.0) on modified CPE

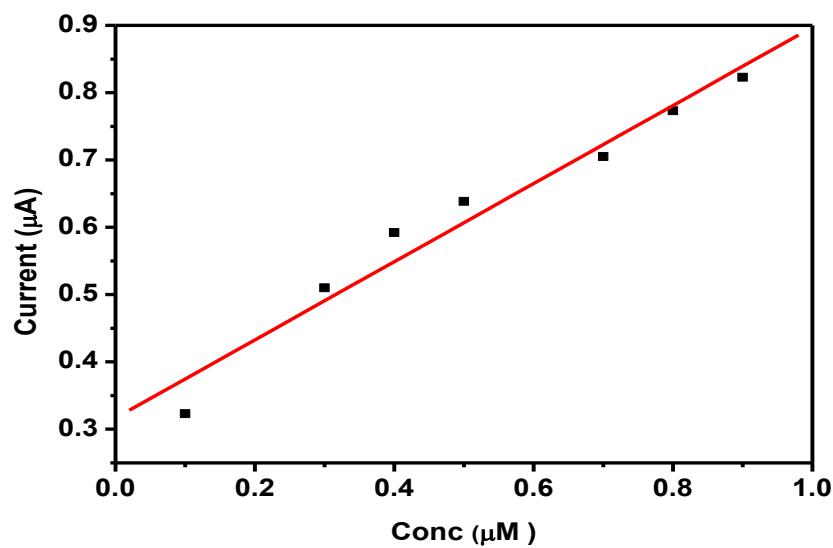


Fig. 6 Calibration Curve of ESO at modified CPE

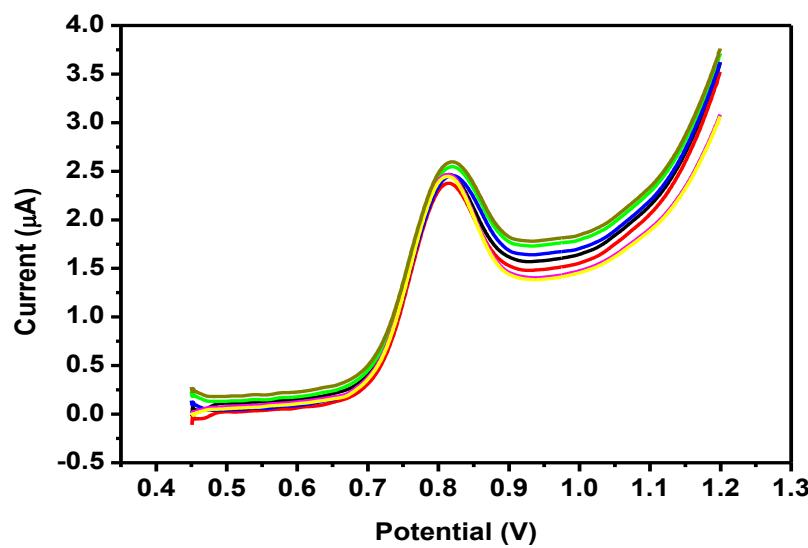


Fig. 7 Linear sweep voltammograms of six successive measurements of 5×10^{-5} M ESO in BR buffer (pH=7.0) using modified CPE