

# Determination of Oxomemazine Hydrochloride by Differential Pulse Voltammetry and Adsorptive Square-Wave Voltammetry at Glassy Carbon Electrode in Pure Form and Pharmaceutical Formulations

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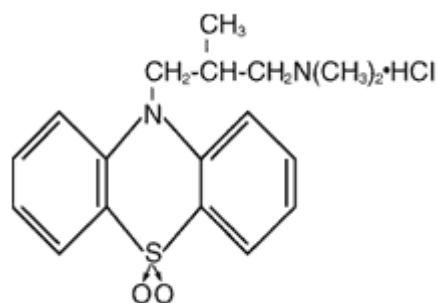
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**Abstract:** Accurate voltammetric methods determinations of Oxomemazine hydrochloride are presented at glassy carbon electrode by cyclic, differential pulse and square wave voltammetry (CV, DPV and SWV, respectively). Based on the anodic oxidation peak at approximately 0.898 V in 0.04M B-R buffer (pH 8.0) Cyclic voltammetric studies indicated the oxidation of Oxomemazine hydrochloride at the electrode surface through a single one-electron irreversible step and fundamentally controlled by adsorption. The oxidation peak was used to determine Oxomemazine hydrochloride in range 1.25  $\mu\text{M}$  - 10 $\mu\text{M}$  ( $r^2=0.9903$ ) and 0.37 $\mu\text{M}$  - 4.5 $\mu\text{M}$  ( $r^2=0.9924$ ) by DPV and SWV respectively. The procedure was successfully applied for the assay of Oxomemazine hydrochloride in syrup (toplexil)<sup>®</sup>. The percentage recoveries were in agreement with those obtained by the reference method.

**Keywords:** Oxomemazine, differential pulse, Square-wave adsorptive Voltammetry, Glassy carbon electrode.

## 1. Introduction

Oxomemazine is an 3-(5,5-dioxo-phen-othia-zin-10-yl)-N,N,2-trimethyl-propanaminium chloride antihistamine and anticholinergic of the phenothiazine chemical class used for the treatment of cough. Fig. 1 shows the chemical structure of OXM. Many methods have been described for OXM determination, such spectrophotometry [1,2], liquid chromatography [3] and potentiometric sensors [4]. Voltammetric analytical methods have been used for the detection of a wide range of drug compounds due to their selectivity, sensitivity, and relatively reduced time consumption compared to other analytical techniques. Additional application of electrochemistry includes the determination of Redox properties of drugs and electrode mechanism. Redox properties of drug molecules can give explanation to their metabolic fate processes or pharmacological activity. Among electrochemical methods, OXM has been assessed by voltammetry using glassy carbon electrode (GCE). GCE is widely used as an electrode material in electrochemistry, as well as for high temperature crucibles and as a component of some prosthetic devices, and can be fabricated as different shapes, sizes and sections. The aim of this work describes the development of a simple, rapid and selective voltammetric method to directly determine the OXM concentration in pure and pharmaceuticals formulations at glassy carbon electrode using cyclic, differential voltammetry (DPV) pulse and square wave voltammetry (SWV).



**Figure 1:** Chemical structure of Oxomemazine hydrochloride (OXM)

## 2. Experimental

### 2.1. Apparatus

All voltammetric experiments were performed using a Metrohm computrace voltammetric analyzer model 797 VA with Software Version 1.0 (Metrohm Switzerland) is the name of the control software for the PC-controlled 797 VA Computrace System for voltammetric analysis. With a three-electrode configuration: glassy carbon disc electrode as working electrode (mini glassy carbon disk electrode of the active zone: 2.8 mm, for ELCD 641/656), a Ag/AgCl (3 ML-1 KCl) as reference electrode and a platinum wire counter electrode were used. The pH was measured using 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.

## 2.2. Chemicals and Solutions

All chemicals and reagents used were of analytical reagent grade and some of them were used as such without any further purification. Distilled water was used throughout all experiments. Oxomemazine hydrochloride (OXM) standard and pharmaceutical formula (toplexil) was kindly Sanofi in Egypt (Zietoun, Cairo, Egypt), Egypt. Stock solutions of  $10^{-3}$  M was prepared by dissolving an appropriate weighed of OXM in 25ml bidistilled water then complete the appropriate volume (100ml) with bidistilled water. The stock solution was stored in a refrigerator. Britton - Robinson (BR) buffer solutions (2.0-12) were used as supporting electrolyte. All solutions were prepared by using analytical grade reagents in bidistilled water.

## 2.3. Working Electrode

To improve the sensitivity and resolution[5] of the voltammetric peaks, Before each measurement, the glassy-carbon surface was polished with alumina (BAS CF-1050) on an alumina polish pad (BAS MF-1040) for 60 s and then rinsed with purified water and gently dried with a tissue paper. The supporting electrolyte was placed in the cell and several potential sweeps were applied to obtain a low background.

## 2.4. Construction of Calibration Curve

Aliquots of OXM were transferred [6-7] to 25-ml volumetric flasks and were completed to the mark with B-R buffer pH 9. The solution was then transferred into a voltammetric cell, and pure  $N_2$  gas was passed for 2 min. Square-wave and differential pulse voltammograms were then recorded in the range of 0 to 1.0 V. The calibration graph obtained with a known concentration of OXM was used to convert peak current into sample concentrations. The recovery was calculated using the standard addition method.

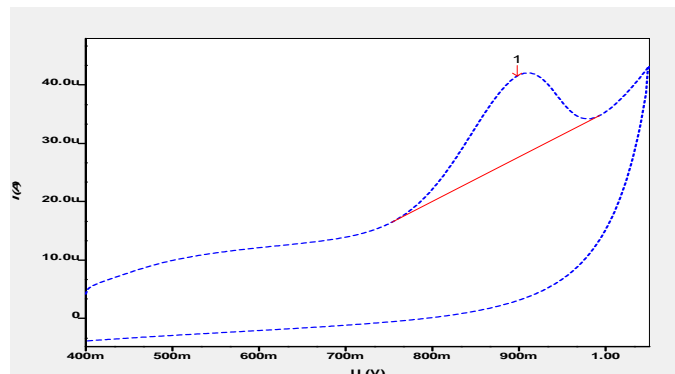
## 2.5. Analysis of Pharmaceutical Dosage Form

The syrup having OXM has been obtained by adding bi distilled water up to 50% of the excipient volume. Stir the syrup for 10 min then filtrate and complete appropriate volume with bi distilled water, syrup were subsequently diluted so that OXM concentration lies in the range of calibration plot. voltammograms were then recorded under exactly identical conditions that were employed while recording voltammograms for plotting calibration plot.

## 3. Results and Discussion

### 3.1. Cyclic voltammetry of OXM

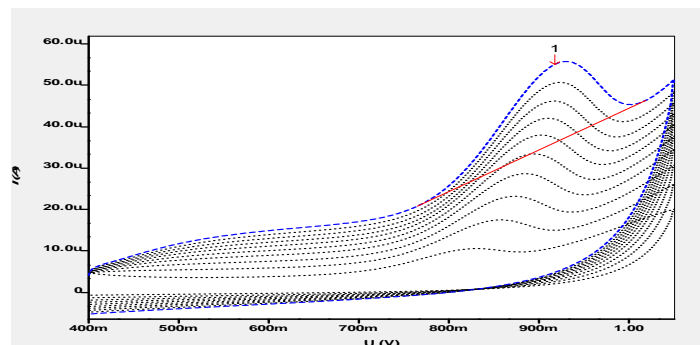
Figure 2 shows the cyclic voltammograms of  $5\mu\text{M}$  OXM at GC in B-R buffer electrolyte solutions at pH=8. The voltammograms were obtained at  $100\text{ mV/s}$ . with scan rate  $100\text{ mV/s}$  exhibited a well-defined and reproducible anodic with no peak on the reverse scan, suggesting the irreversible nature of the electrode reaction in the cathodic scan.



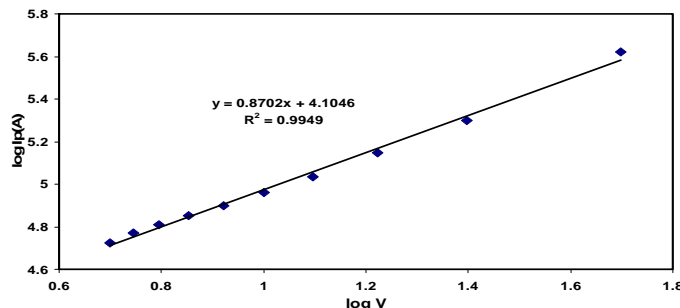
**Figure 2:** Cyclic voltammograms of  $5\mu\text{M}$  OXM at GCE at scan rates from  $100\text{ mV s}^{-1}$  in  $0.04\text{ M}$  B-R buffer (pH 8.0).

### 3.2. Effect of Scan Rate

The relationship between the measured peak current and scan rate was studied over range  $20\text{--}200\text{ mV s}^{-1}$ . It was found to be directly proportional the peak current and the peak potential of OXM were evaluated as in Fig. 3. The positive shifts in the peak potential together with no cathodic wave confirmed the irreversibility of the oxidation process. Fig. 4 shows a plot of logarithm of peak current versus logarithm of scan rate gave a straight line with a slope of 0.8702 (correlation coefficient 0.9949), close to the theoretical value of 1.0, [8,9] which is expected in this case redox process had adsorption reaction component so the reaction influenced by adsorption time and adsorption potential.



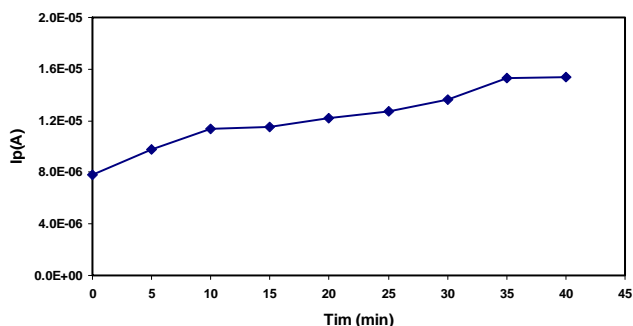
**Figure 3:** Cyclic voltammograms of  $5\mu\text{M}$  OXM at GCE at different scan rates from  $20\text{--}200\text{ mV s}^{-1}$  in  $0.04\text{ M}$  B-R buffer (pH 8.0).



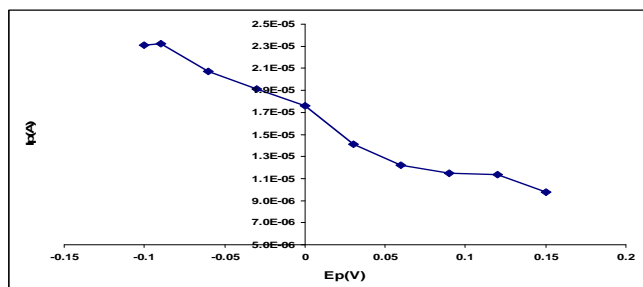
**Figure 4:** Dependence of CV anodic peak current logarithm,  $\log I_p$ , of  $5\mu\text{M}$  OXM at GCE in  $0.04\text{ M}$  B-R buffer at pH 8.0

### 3.3. Effect of accumulation time and potential

The accumulation [10] of OXM at GCE surface depends on operational factors, which were precious additional investigations to ensure sensitive detections of this drug. So, the effect of accumulation time on the efficiency of the collection of 5 $\mu$ M OXM drug on the working electrode surface was evaluated by rising the accumulation time over the range of 0–40s. The resulting peak current- optimum accumulation time is exhibited in 40s as in Fig. 5 and as can be seen from this plot, a steady enhancement in the peak current was observed over the range 0–40 s and after that the peak intensity nearly decreased probably due to the saturation of the GCE surface. Hence, 40s accumulation time was selected for all the future experiments. On the other hand, variance of the accumulation potential over the range from 0.15 to -0.1 V Fig. 6 at 40 s accumulation time revealed that a pre concentration potential of 0.1 V was the optimum condition.



**Figure 5:** Effect of accumulation time ( $T_{acc}$ ) of 5 $\mu$ M OXM peak current at B–R buffer, pH = 8,  $E = -0.1$ V and scan rate 100mVs $^{-1}$



**Figure 6:** Effect of accumulation potential ( $E_{ac}$ ) 5 $\mu$ M OXM peak current at B–R buffer, pH = 8, time 35s and scan rate 100mVs $^{-1}$

### 3.4. Effect of pH

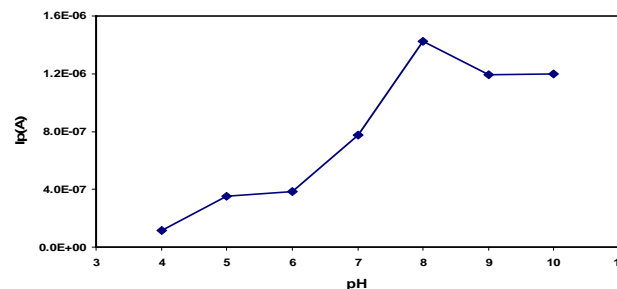
pH is one of the important parameters that affected the electrode response in drug sample determination, The shape and electrochemical behavior of 20 $\mu$ M OXM in 0.04M B-R in the range 3.0–10.0 electrolyte solution at different pH values and cyclic voltammetry was studied at GCE, the pH of the solution strongly affects the peak current and potential ( $E_p$ ) as in Figs (7, 8) It can be seen that the anodic peak current of OXM reaches a maximum value at pH = 8.0, and then decreases gradually as pH increases Fig. 7. Therefore, pH = 8.0 was chosen as optimum pH for the following electrochemical detection of OXM. On the other hand the

anodic peak potential of OXM at the surface of GCE shift to less positive [11-13] values linearity with increasing pH of the buffered solution as in Fig. 8.

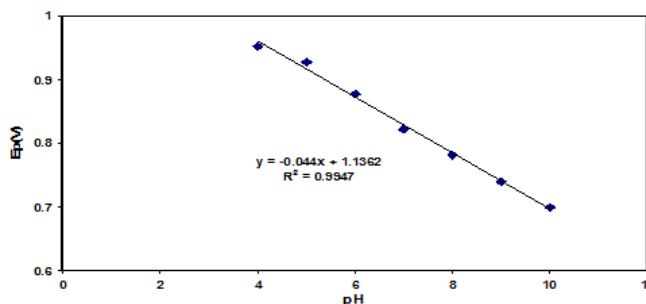
The pH dependences of the peak potentials are expressed as follows:

$$E_0 = -0.044\text{pH} + 1.1362 \quad R^2 = 0.9947$$

This slope 0.044 V/pH is indicated that which 25 °C was close to the theoretical value of  $-59 \text{ mVpH}^{-1}$  at this result was agreement with the Nernst equation for a one proton coupled reversible single electron transfer.



**Figure 7:** The relationship of anodic peak current response vs. solution pH value of 5 $\mu$ M OXM solution in B-R buffer on GCE at a scan rate 100 mVs $^{-1}$ .



**Figure 8:** The relationship of  $E_p$  vs. solution pH of 5 $\mu$ M OXM at GCE electrode at a scan rate 100 mVs $^{-1}$

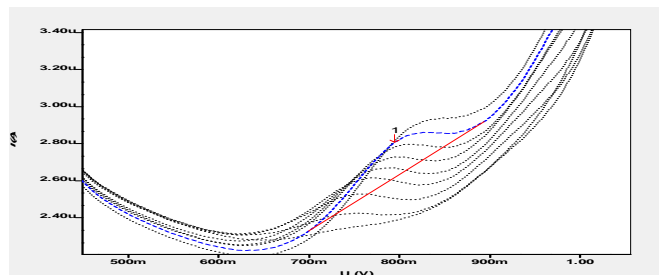
### 3.5. Analytical applications

#### 3.5.1 Differential Pulse voltammetry

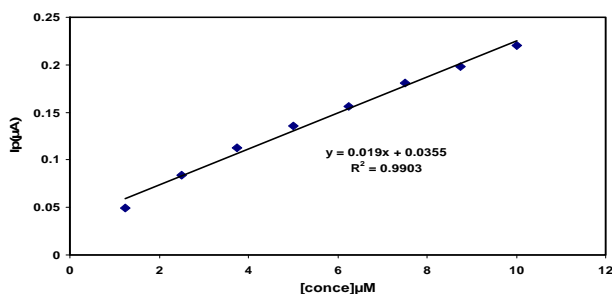
To develop a Quantitative voltammetric evaluation methodology for determining the drug is established on the linear correlation between the peak current and concentration. For analytical purposes we selected the DPV and SWV mode. Differential pulse experiments were performed on the GCE in B-R buffer solution at pH = 8 with experimental conditions were: scan rate 5 mV/s; pulse amplitude 50 mV; sample width of 40 ms; pulse width of 50 ms; and pulse period 40 ms. The potential was scanned anodically from an initial to a final potential of 500 - 1000 mV resulting voltammograms shown in Fig. 9 show that while the peak potential remained almost constant at 0.809V. The DVP data for the determination of the drug under investigation in Fig. 10 shows a linear relation between the peak current ( $I_p$ ) and OXM concentration ( $C$ ) were found in the following range: 1.25  $\mu$ M - 10 $\mu$ M. The calibration plots were described by the following equations:

$$I_p = 0.019C (\mu\text{M}) + 0.0355$$

r (Correlation coefficient) = 0.9903



**Figure 9:** Background corrected DPV response for different concentrations of OXM 1.25 μM - 10 μM in BR buffer solution (pH 8.0) at GCE



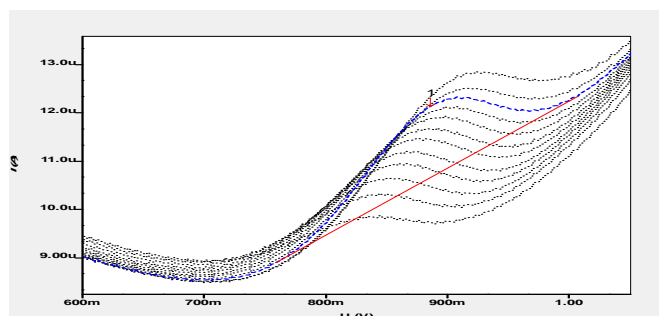
**Figure 10:** Differential pulse voltammetric responses for successive additions of OXM from 1.25 μM - 10 μM in BR buffer solution (pH 8.0) at GCE

### 3.5.2 Square wave voltammetry

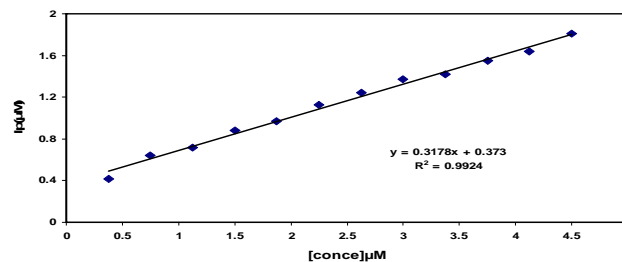
SWV experiments were performed at the GCE in B-R buffer solution at pH = 8 with experimental conditions were: scan rate 100 mV/s; pulse amplitude 20 mV; , 2 mV potential step and potential range of 500 to 1000 mV and frequencies 50 Hz. The potential was scanned anodically from an initial to a final potential of 600 - 1000 mV resulting voltammograms shown in Fig. 11 shows that while the peak potential remained almost constant at 0.866V. The SWV data for the determination of the drug under investigation in Fig. 12. Shows linear relations between the peak current (Ip) and OXM concentration (C) were found in the following range: 0.37 μM - 4.5 μM. The calibration plots were described by the following equations:

$$I_p = 0.317C (\mu M) + 0.373$$

r (Correlation coefficient) = 0.9924



**Figure 11:** Background corrected SWV response for different concentrations of OXM 0.37 μM - 4.5 μM in BR buffer solution (pH 8.0) at GCE



**Figure 12:** Square wave voltammetric responses for successive additions of OXM from 0.37 μM - 4.5 μM in BR buffer solution (pH 8.0) at GCE.

### 3.6. Validation of the Analytical Procedure

The linearity of the calibration curve was obtained for both DPV and SWV techniques as in above these concentration range and the loss of linearity was probably due to the adsorption of OXM on the electrode surface. The characteristics of these graphs are given in Table 1. The precision of the method was investigated by repeatedly (n = 5) measuring peak potential and peak current of OXM within a day and over three consecutive days for both techniques. LOD and LOQ were calculated as (3 s/m) and (10 s/m), respectively where s is standard deviation of response (five runs) and m is the slope of the calibration curve. LOD and LOQ values confirmed the sensitivity of the proposed methods, These results demonstrated good precision and accuracy [14, 15].

**Table 1:** Characteristics of PNT calibration plots using proposed voltammetric methods

Parameters	DPV	SWV
Slope (mV decade <sup>-1</sup> )	0.019	0.317
Intercept (mV)	0.0355	0.373
Correlation coefficient	0.9903	0.9924
Detection limit (μmol L <sup>-1</sup> )	0.365	0.053
Limit of quantitation (μmol L <sup>-1</sup> )	1.219	0.177
Working pH	8	8
Concentration range, μmol L <sup>-1</sup>	0.37 - 4.5	0.37 - 4.5
Average recovery (%)	99.85-99.95	99.84-99.95
RSD% a	0.021	0.0079

### 3.7. Application to Analysis of Pharmaceuticals

On the aim of these results, both proposed methods (DPV and SWV) were applied to the direct determination of OXM in syrup [16, 17], using the related calibration curve of the straight lines without sample preparation and after an adequate dilution Table 2. The proposed analysis procedure was successfully applied for the assay of OXM in its pharmaceutical formulations. As far as we know, there is no official method in any pharmacopoeias related to pharmaceutical preparations of OXM. For this reason, the HPLC method [18] was used for compare son and for the reliability of the developed procedures. The results obtained for the formulation are listed in Table 2 and compared with the HPLC. The recovery studies were carried out by adding the known amount of the pure drug to the earlier analyzed pharmaceutical formulations of OXM. The recovery [19] of the drug was calculated by comparing the concentration



obtained from the spiked mixtures with those of the pure drug. Table 2 shows a good result demonstrates the selectivity of the proposed method for the determination of OXM in commercial tablet forms.

**Table 2:** Evaluation of the accuracy and precision of the proposed and official methods for the determination of OXM In its pharmaceutical forms at GCE

Pantoloc	[Drug]	Proposed method ±%RSD, n=5	Official method ±%RSD, n=5	F-test	T-test
DVP	33mg	100.02 ± 0.12	99.91± 1.3	1.13	2.04
SWV	33mg	100.01 ± 0.11	100.05± 1.08	1.22	2.06

#### 4. Conclusion

DPV and SWV methods have been developed for the determination of OXM in pure form and pharmaceutical formulation. The principal advantage of the proposed method over the reference HPLC method is sensitivity and specificity. The proposed voltammetric technique has the advantages of being simpler, faster, more selective and more cost-effective than other technique. DPV and SWV methods are rapid, requiring about 5 min to run the sample. The possibility of monitoring the compound in pharmaceutical formulation makes the voltammetric method useful for pharmacodynamic purposes.

#### Acknowledgement

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