Determination of Olanzapine in Pharmaceutical Preparations by Linear Sweep Voltammetry Method

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Abstract

In this study, simple and fast linear sweep voltammetry method was developed and validated for determination of olanzapine in pharmaceutical preparations. The proposed method was based on electrochemical oxidation of olanzapine on glassy carbon electrode in solution containing 0.04 M Britton-Robinson buffer of pH 1.65. The well-defined an oxidation peak was observed at 1.06 V. The calibration curve was linear for olanzapine at the concentration range of 2.5-50 μg/mL for linear sweep voltammetry method. Intra- and inter-day precision values for olanzapine were less than 4.78, and accuracy (relative error) was better than 1.85%. The limits of detection and quantification of olanzapine were 0.50 and 1.50 μg/mL, respectively. The mean recovery of olanzapine was 99.8% for pharmaceutical preparations. Stability measurements were carried out with linear sweep voltammetry method. The results were evaluated comparing these measurements with those of standards and expressed as percentage deviation and olanzapine was found as stable at room temperature, 4 and -20 °C for at least 72 h. No interference was found excipient at the selected assay conditions. The voltammetric run time of 1 min allows the analysis of a large number of samples in a short period of time. The proposed method is highly sensitive, precise and accurate and can be used for the reliable quantitation of olanzapine in pharmaceutical dosage form.

Keywords—Cyclic voltammetry, Linear sweep voltammetry, Olanzapine, Validation

1 Introduction

Olanzapine (Figure 1) belongs to the new generation of neuroleptic drugs used in the treatment of schizophrenia. These new drugs are atypical because there is a better possibility of obtaining a sufficient clinical response without extrapyramidale side-effect with this class than the conventional drugs. Typical neuroleptic drugs treat the positive symptoms of psychosis (hallucinations, paranoi, and delusions) but are largely ineffective in treating many of the negative symptoms (low levels of interest, lack of motivation, social withdrawal, and poverty of speech). The most recent atypical antipsychotic drug to become commercially available is olanzapine. This is a very active drug and is administered at very low dosages[1].

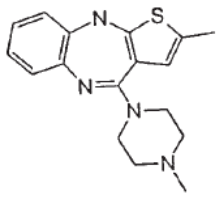

Figure 1: Chemical structure of olanzapine.

Several methods have been reported for the determination of olanzapine including high performance liquid chromatography with electrochemical [2-5], UV detection [6-8], amperometric detection [9], tandem mass spectrometry [10-13] and capillary zone electrophoresis [14] in body fluids and in tablet forms.

The reported methods were influenced by interference of endogenous substances and potential loss of drugs in the re-extraction procedure and involving lengthy, tedious and time-consuming plasma sample preparation and extraction processes and requiring a sophisticated and expensive instrumentation.

The development of a new method capable of determining drug amount in pharmaceutical dosage forms is important. Electroanalytical techniques have been used for the determination of a wide range of drug compounds with the advantages that there are, in most, instances no need for derivatization and that these techniques are less sensitive to matrix effects than other analytical techniques. Additionally, application of electrochemistry includes the determination of electrode mechanism. Redox properties of drugs can give insights into their metabolic fate or their in vivo redox processes or pharmacological activity [15-18]. Despite the analytical importance of the electrochemical behavior and oxidation mechanism of olanzapine, no report has been published on the voltammetric study of the electrochemical oxidation of olanzapine in aqueous media. Therefore, the goal of this work was the development of new a linear sweep voltammetry (LSV) method for the direct determination of olanzapine in pharmaceutical preparations without any time-consuming extraction or evaporation steps prior to drug assay. This paper describes fully validated simple, rapid, selective and sensitive procedures for the determination of olanzapine employing LSV methods on the glassy carbon electrode. Besides, the method was successfully applied for the quality control of a commercial olanzapine quantify the drug and to check the formulation content uniformity.

2 Experimental

2.1 Chemical and reagents

Olanzapine was purchased from Fluka (Buchs, Switzerland). Ollafax tablets were obtained from pharmacy (Erzurum, Turkey). 0.5 M H_2SO_4, 0.2 M phosphate buffer between pH 2 and 12, 0.04 M Britton-Robinson buffer between pH 1.5 and 12 and 0.2 M acetate buffer between pH 3.5 and 5.7 were used as the supporting electrolytes.

2.2 Electrochemical instrumentation

Voltammetric measurements were obtained with Gamry Potentiostat Interface 1000 controlled with software PHE 200 and PV 220. A three electrode cell system was used a glassy carbon electrode (Φ= 3 mm, BAS) as working electrode and an Ag/AgCl (KCl 3M, BAS) electrode as the reference electrode. All the results in the figures are presented in respect to the Ag/AgCl, 3M KCl reference electrodes. Before each experiment, the glassy carbon surface was polished with polishing alumina (prepared from 0.01 μm aluminium oxide) on alumina polish pad then rinsed with purified water.

2.3 Procedure for pharmaceutical preparations

A total 10 tablets of olanzapine (Ollafax) were accurately weighed and powdered. An amount of this powder corresponding to one tablet olanzapine content was weighed and accurately transferred into 100 mL calibrated flask and 50 mL of 0.04 M Britton-Robinson buffer (pH 1.65) was added and then the flask was sonicated to 10 min at room tempature. The flask was filled to volume with 0.04 M Britton-Robinson buffer (pH 1.65). The resulting solutions in both the cases were filtered through Whatman filter paper no 42 and suitably diluted to get final concentration within the limits of linearity for the respective proposed method. The drug content of olanzapine in tablet was calculated from the current potential curve.

3 Results and Discussion

3.1 Voltammetric behavior of olanzapine

The electrochemical behavior of olanzapine was investigated at the glassy carbon electrode in 0.04 M Britton-Robinson buffer (pH 1.65) as the supporting electrolyte by using cyclic voltammetry (CV). Figure 2 shows a typical cyclic voltammogram of 30 μg/mL olanzapine recorded under these conditions for the scan rate of 0.1 V/s. In the anodic sweep, an oxidation peak is seen at about potential of 1.06 V.

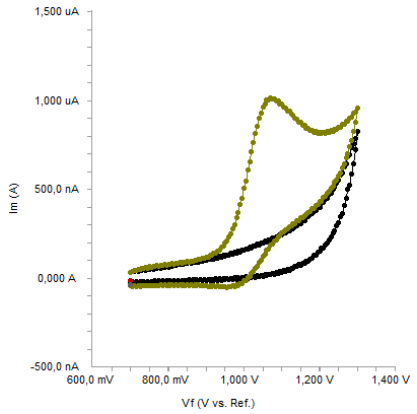

Figure 2: Cyclic voltammogram for the oxidation of 30 µg/mL olanzapine in 0.04 M Britton-Robinson buffer (pH 1.65), scan rate: 0.1 V/s.

In order to gain a deeper insight into the voltammetric waves, the effect of scan rate on the anodic peak currents (İm) and peak potentials (Ep) was studied in the range of 0.01-1 V/s of the potential scan rates in acetonitrile solution containing 10 µg/mL concentration of olanzapine (Figure 3).

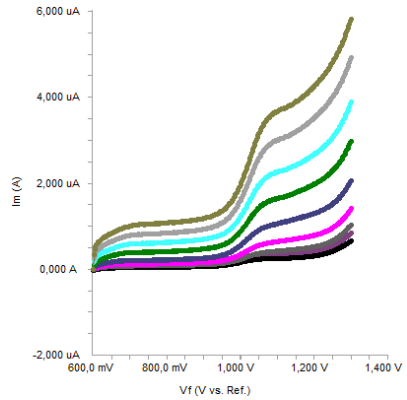

Figure 3: Linear sweep voltammograms for the oxidation of 10 µg/mL olanzapine in 0.04 M Britton-Robinson buffer (pH 1.65) as a function of scan rate.

The representative linear sweep voltammograms obtained at glassy carbon electrode for 10 µg/mL olanzapine as a function of the scan rate are studied. However, the plots of logarithm of peak currents versus logarithm of scan rates for 10 µg/mL concentration of olanzapine display straight lines with 0.47 slope, which are close to theoretical value of 0.5 expected for an ideal diffusion-controlled electrode process [19]. log Im-log ν curve is more eligible for this aim, therefore, a diffusional process for peak should be considered. These results suggest that the redox species are diffusing freely from solution and not precipitating onto the electrode surface. The reason for this behavior may be due to the solubility of the intermediate species in buffer solution or poor adherence of products on the electrode surface. As shown in Figure 3, the oxidation peak potential (Epa) for peaks shift toward more positive values with increasing scan rate. The relationship between the peak potential and scan rate is described by the following equation [20],

$$E_{pa} = E^{0} + RT/[(1-\alpha)n_a F][0.78 + \ln(D^{1/2}k_s^{-1}) - 0.5\ln RT/[(1-\alpha)n_a F]] + RT/[(1-\alpha)n_a F]/2\ln\nu \quad (3.1)$$

and from the variation of peak potential with scan rate αna can be determined, where α is the transfer coefficient and na is the number of electrons transferred in the rate determining step. The slope indicate the value of αna is 1.0 for peak. Also, this value obtained indicate the total irreversibility of the electron transfer processes. This result show that the chemical step is a fast following reaction coupled to a charge transfer.

3.2 Validation of the method

The validation was carried out by establishing specificity, linearity, accuracy, precision, limit of detection (LOD), limit of quantification (LOQ), stability, recovery according to ICH Q2B recommendations [21, 22,23].

3.3 Specificity

The effects of common excipients and additives were tested for their possible interferences in the assay of olanzapine. The simulated and placebo samples were prepared and analyzed. It has not been determined any interference of these substances at the levels found in dosage forms. Excipient that was used in this preparation was the most commonly used by the pharmaceutical industry. The specificity of the method was investigated by observing any interference encountered from the common tablet excepients such as titanium dioxide, sodium chloride, talc, lactose, starch, and magnesium stearate. These excepients did not interfere with the proposed method.

3.4 Linearity

Standard solutions were prepared as 2.5-50 µg/mL (2.5, 5, 10, 20, 30, 40 and 50 µg/mL) for LSV, (Figures 4).

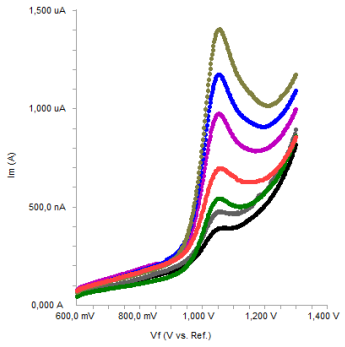

Figure 4: Linear sweep voltammograms for different concentrations of olanzapine in 0.04 M Britton-Robinson buffer (pH 1.65) (2.5, 5, 10, 20, 30, 40 and 50 µg/mL).

Calibration curve was constructed for olanzapine standard by plotting the concentration of compound versus peak current responses. The calibration curves were evaluated by its correlation coefficients. The correlation coefficients (r) of all the calibration curves were consistently greater than 0.99. The linear regression equations were calculated by the least squares method using Microsoft Excel® program and summarized in Table 1.

Table 1.Linearity of Olanzapine.

Method	Range µg/mL	LR[a]	S_a	S_b	R^2	LOD	LOQ
LSV	**2.5-50**	**y=20.911x +339.37**	**3.168**	**0.014**	**0.993**	**0.50**	**1.50**

a:Based on three calibration curves, LR: Linear regression, Sa: Standard deviation of intercept of regression line, Sb: Standard deviation of slope of regression line, R2: Determination of correlation, y: Peak current, x: Olanzapine concentration (µg/mL), LOD: Limit of detection, LOQ: Limit of quantification.

3.5 Accuracy and precision

Accuracy of the assay methods was determined for both intra-day and inter-day variations (intra-day) and intermediate precision (interday). Repeatability refers to the use of the analytical procedure within a laboratory over a short period of time that was evaluated by assaying the QC samples during the same day. Intermediate precision was assessed by comparing the assays on different days (2 days). The intra-day accuracy ranged from 1.68% to 1.85% and precision from 2.04% to 4.78% (Table 2). The results obtained from intermediate precision (inter-day) also indicated a good method precision.

Table 2. Precision and Accuracy of Olanzapine.

Method	Added (µg/mL)	Intra-day			Inter-day		
		Found± SD[a] (µg/mL)	Accur[c]	Preci. RSD%[b]	Found± SD (µg/mL)	Accur[c]	Preci. RSD %[b]
LSV	7.5	7.41± 0.116	-1.11	1.57	7.46± 0.136	-0.44	1.83
	25	24.67± 0.816	-1.33	3.33	25.33± 1.211	1.33	4.78
	45	45.16± 0.983	0.37	2.17	45.83± 1.169	1.85	2.55

[a]SD: Standard deviation of six replicate determinations, [b]RSD: Relative standard deviation, [c]Accuracy: (%relative error) (found-added)/addedx100.

3.6 Limits of detection (LOD) and quantification (LOQ)

The LOD and LOQ of olanzapine by the proposed method was determined using calibration standards. LOD and LOQ values were calculated as 3.3 σ/S and 10 σ/S, respectively, where S is the slope of the calibration curve and σ is the standard deviation of y-intercept of regression equation (n=6) [22]. The LOD and LOQ values of the methods were summarized in Table 1.

3.7 Stability

To evaluate the stability of olanzapine, standard solutions were prepared separately at concentrations covering the low, medium and higher ranges of calibration curve for different temperature and times. These solutions were stored at room temperature, refrigeratory (4 °C) and frozen (-20 °C) temperature for 24 h and 72h. Stability measurements were carried out with LSV method. The results were evaluated comparing these measurements with those of standards and expressed as percentage deviation and olanzapine was found as stable at room temperature, 4 and -20 °C for at least 72 h (Table 3).

Table 3. Stability of Olanzapine in Solution.

Stability (%)		Room temperature stability, (Recovery % ± RSD)		Refrigeratory stability, +4°C (Recovery % ± RSD)		Frozen stability, -20°C (Recovery % ± RSD)	
Meth.	Add. (µg/mL)	24 h	72 h	24 h	72 h	24 h	72 h
LSV	10	96.7 ±2.16	98.4 ±2.46	98.2 ±0.74	97.4 ±2.32	98.3 ±2.28	102.1 ±1.86
	25	98.8 ±1.92	99.1 ±2.41	101.2 ±3.09	99.8 ±1.06	96.4 ±2.21	99.4 ±2.92
	50	100.8± 3.64	98.6 ±2.65	99.3 ±2.18	98.6 ±1.52	97.7 ±3.16	99.7 ±1.68

3.8 Recovery

To determine the accuracy of the LSV method and to

study the interference of formulation additives, the recovery was checked as three different concentration levels. Analytical recovery experiments were performed by adding known amount of pure drugs to pre-analyzed samples of commercial drug form. The recovery values were calculated by comparing concentration obtained from the spiked samples with actual added concentrations. These values are also listed in Table 4.

Table 4. Recovery Values of Olanzapinee in Pharmaceutical Preparation.

Method	Ollafax (µg/mL)	Added (µg/mL)	Found ±SD (µg/mL)	Recovery (%)	RSD (%)
LSV	15	5	4.97± 0.201	99.4	4.04
		15	15.10± 0.517	100.7	3.42
		35	33.85± 0.941	96.7	2.78

4 Conclusion

In the present report, a simple, rapid, reliable, specific, accurate and precise LSV method was developed and validated for the determination of olanzapine in pharmaceutical preparations. The method described has been effectively and efficiently used to analyze olanzapine pharmaceutical preparations without any interference from the pharmaceutical excipients. The voltammetric run time of 1 min allows the analysis of a large number of samples in a short period of time. Therefore, the methods can be used effectively without separation for routine analysis of olanzapine in pure form and its formulations.

5 Referanslar

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