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Determination of atorvastatin at pharmaceutical tablet using cyclic voltammetry technique

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Abstract

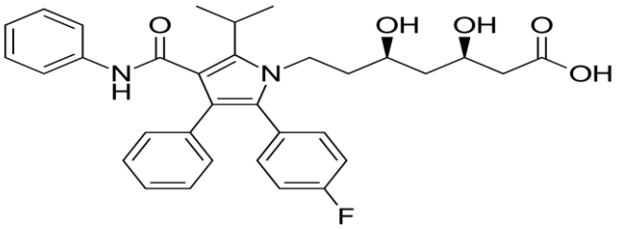
Voltammetric oxidation behavior of atorvastatin (ATOR) was studied using cyclic voltammetry in phosphate buffer at pH3. The glassy carbon electrode was used to accumulate ATOR into its surface to give a well-defined oxidation peak at 0.95V potential in presence of Ag/AgCl reference electrode and Pt auxiliary electrode. The high sensitivity of ATOR determination using cyclic voltammetry, was observed with optimum parameters such as: phosphate buffer, pH3, 30 s accumulation time, 0.0 V accumulation potential and 100 mV s-1 scan rate, so these parameters were chosen for the next experiments. The repeatability, stability, calibration curve and detection limit were studied to evaluate the analytical performance for the CV method. Repeatability of $6x10^{-5}$ mol L^{-1} of ATOR was reported 0.22% relative standard deviation (RSD%) for ten anodic CV measurements. The stability was monitored for $6x10^{-5}$ mol L^{-1} ATOR signal for 90 min, yielded a good stability was recorded for the ATOR determination at the voltammetric period. Calibration curve was studied over the range $1x10^{-5}$ — 6×10^{-5} mol L^{-1} for ATOR drug to be obtained a linear relationship with 0.998 correlation coefficient (r^2) for sex measurements (n=6). Detection limit (LOD) was calculated to be 7.25×10^{-8} mol L^{-1}(0.04 ppm). Cyclic voltammetry technique was applied for the determination of ATOR at the commercial tablet.

Keywords: Cyclic voltammetry, oxidation, atorvastatin, commercial tablet, GC electrode, phosphate buffer.

1.Introduction

Electrochemical techniques can easily be adopted to solve many problems of pharmaceutical interest with a high degree of accuracy, precision, sensitivity and selectivity, often in spectacularly reproducible way by employing an analytical approach[1-8]. Voltammetry, an electrochemical analytical method for assessing the current with a function of differential electrochemical reducing potentials possesses better sensitivity and applicability. Voltammetric technique–based evaluation works on the fact that current flowing through the system is a function of potential applied across the electrodes. Briefly, in voltammetric methods, the range of potentials are scanned where the generated current is directly proportional to the concentration of electroactive species present in the sample[9]. Voltammetric methods give high sensitivity and wide linear dynamic range characterization using voltammetric techniques determines various properties of the equilibrium constant in coupled reactions materials used in the biosensing probe such as electrochemical reversibility, and electron transfer, in voltammetry electrons are added to or removed from compounds by electric fields. This field is generated by application of voltage across an electrode/solution interface. At a critical voltage (dependent on the compound, electrode, and electrolyte) the chemical present at the electrode surface surrenders its electrons to the electrode, resulting in a small flow of current[10]. If the polarity of the field is reversed the electrons can be returned from the electrode to the oxidized compound, reverting it to its original state different compounds in a mixture may require different levels of field in order to oxidize thus, by gradually increasing the field strength (by scanning the voltage) one can oxidize several compounds separately the resulting current from the electrode may then have distinct peaks, each the oxidation of a single chemical[11]. Generality voltammetry is very specific, in that it is only applicable to molecules that are electrochemically active. This includes the catecholamine and indoleamine neurotransmitters and their metabolites, as well as ascorbic and uric acid. The specificity is an asset when the monitoring is to be done without any prior chemical separation, but of course limits the utility of the method. We have found voltammetry to be most useful when coupled to short-term, well-defined stimuli such as brief electrical stimulation. When a longer-term stimulus such as drug administration is used, interpretation of the observed oxidation current is complicated by shifting baselines and metabolic changes that occur over the course of the measurements[12]. Cyclic voltammetry is a simple extension of the linear sweep technique, one simply adds the reversal scan. This technique retains the best features of two powerful, complementary methodologies. Conventional cyclic voltammetry is especially informative about the qualitative aspects of an electrode process. However, the response waveforms lend themselves poorly to quantitative evaluations of parameters. Cyclic voltammetry retains the diagnostic utility of conventional cyclic measurements, but it does so with an improved response function that permits quantitative evaluations as precise as those obtainable with the usual alternating current approaches. Although this technique is not widely employed, it can be a useful adjunct to direct current cyclic voltammetry[13]. Cyclic voltammetry is a very useful technique to monitor the growth of an electropolymerized film and to evaluate its thickness. During the continuous growth of the polymer layer at an inert substrate (gold or glassy carbon electrodes) the current density at the redox peaks of the electroactive polymer increases continuously[14]. CV is mainly used for studying the reversibility of electrode processes and for kinetic observations, and only sometimes for analytical purposes. CV gives information on the redox behavior of electrochemically active species and on the kinetics of electrode reactions as well as offering the possibility of identifying reactive intermediates or subsequent products. And it's are based on recording the current during a linear change of voltage at a stationary working electrode[15]. There are many published articles using cyclic voltammetry technique for the determination organic and inorganic compounds [16- 21]. Atorvastatin, (Scheme1) an antihyperlipoproteinemic drug, inhibits 3-hydroxy-3 methylglutaryl, a key enzyme in the biosynthesis of cholesterol. The IUPAC name is (3R,5R) -7- [2-(4-Fluorophenyl)-3-phenyl-4 (phenylcarbamoyl) 5-propan-2-lpyrrol-1-yl]-3,5-dihydroxyheptanoic acid and the formula is $C_{33}H_{35}FN_2O_5$, the molar

mass is 558.64 g·mol^{-1}. Atorvastatin was patented in 1986 and approved for medical use in the United States in 1996[22]. Using of atorvastatin leads to reducing the total cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, triglycerides levels, and C-reactive protein as well as increasing high density lipids (HDL) levels [23,24]. This drug also stabilizes plaque and prevents risk of strokes, heart attack or other heart complications through anti-inflammatory and other mechanisms.



Scheme 1. Structural of formula of atorvastatin

2. Experimental

2.1 Apparatus

A 797 VA instrument (Switzerland made, Metrohm company) was used for the voltammetric determinations of ATOR in commercial tablet. VA instrument is connected with three electrodes system including GC working electrode, Ag/AgCl (3 mol L^{-1} KCl) reference electrode and platinum auxiliary electrode. The pH measurements were carried out using digital pH-meter (model pH211, Hanna company). The distilled water was prepared using Millie-Q Plus system water purification system (Milford company, USA). The human plasma and urine biological fluids were centrifuged using a labofuge 200 instrument (Heraeus Sepatech company, Germany).

2.2 Chemicals

Atorvastatin (ATOR) standard material was obtained from Qassim Pharma-ceutical co., (Spimaco) Boraidah-KSA. The stock solution of ATOR was prepared by dissolving ATOR in methanol at 50 mL volumetric flask. The diluted ATOR solutions were prepared in methanol solvent according to the requested experimental in different concentrations. Britton-Robinson (B-R), phosphate, and acetate buffers were prepared for the study cyclic voltammetric behavior for ATOR drug to obtain a well oxidation signal [25].

2.3 Procedures

A 10 mL of buffer solution was injected in electrochemical cell after cleaning by acids and distilled water before any additions. Oxidation scan was applied for all measurements over the range of potential 0.0 to 1.2 V. All solutions were purged using nitrogen gas for 100 s period with stirring. The anodic cyclic voltammograms for the determination of ATOR were obtained using the optimum parameters; phosphate pH3, 30 s accumulation time, 0.0 V accumulation potential and 100 mVs^{-1} scan rate. All electrochemical measurements were made at room temperature.

2.3.1 Preparation of pharmaceutical tablet

Five tablets of "Lorvast 40 mg (manufactured by Tabuk pharmaceutical Mfg. Co. Tabuk-Saudi Arabia)" were crushed and weighted by sensitive balance to prepare stock solutions of ATOR (1x10^{-3} mol L^{-1}) which prepared from these tablets, using methanol as a solvent in 50 ml volumetric flask.

3. Results and discussion

3.1. Effect of buffer solution

The nature of the buffer electrolyte is important factor which strongly influence the stability of the analyte and its anodic oxidation and adsorption processes. Among the various investigated buffers (phosphate, acetate and B-R), the best voltammetric signal in terms of sensitivity and resolution have been secured using phosphate buffer pH 3 (see figure 1)

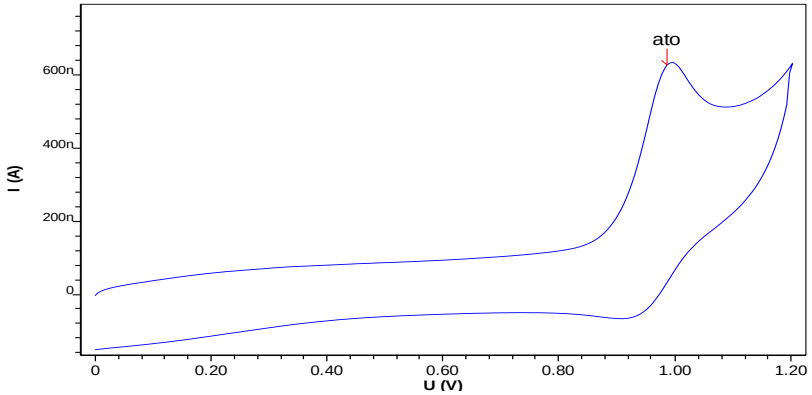
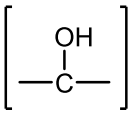
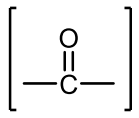
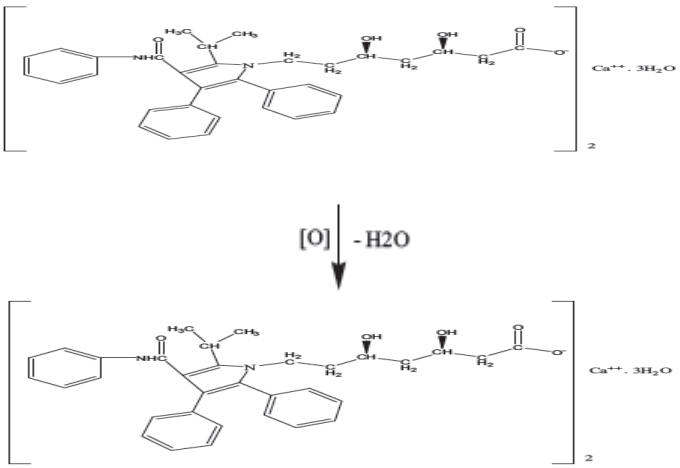


Figure 1. Cyclic voltammogram of 6 x10^{-5} mol L^{-1} of atorvastatin in phosphate buffer pH3

3.2. Oxidation cyclic voltammetry of ATOR

The CV behavior of atorvastatin was investigated in phosphate buffer pH3 and 100mVs^{-1}. The suggested mechanism for atorvastatin oxidation is reported as in scheme 2, where the hydroxyl group  in the atorvastatin formula was oxidized to carbonyl group  [26].



Scheme 2. The proposed mechanism of electrochemical oxidation for atorvastatin drug

3.3 Analytical performance

3.3.1. Calibration curve

A very good linear correlation was obtained between the monitored voltammetric peak current and (ATOR) concentration over the range 1 $x10^{-5}$ - $6x10^{-5}$ mol L^{-1} at phosphate buffer pH3, as shown in figures 2 and 3.

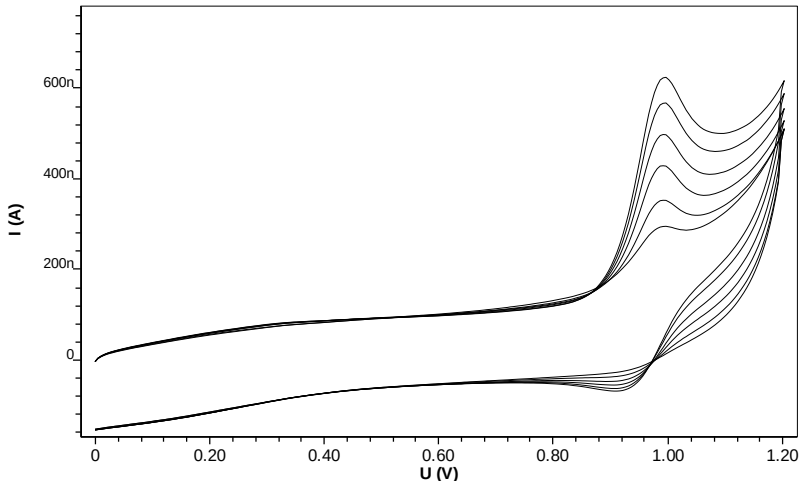


Figure 2. Cyclic voltammograms of atorvastatin for calibration curve

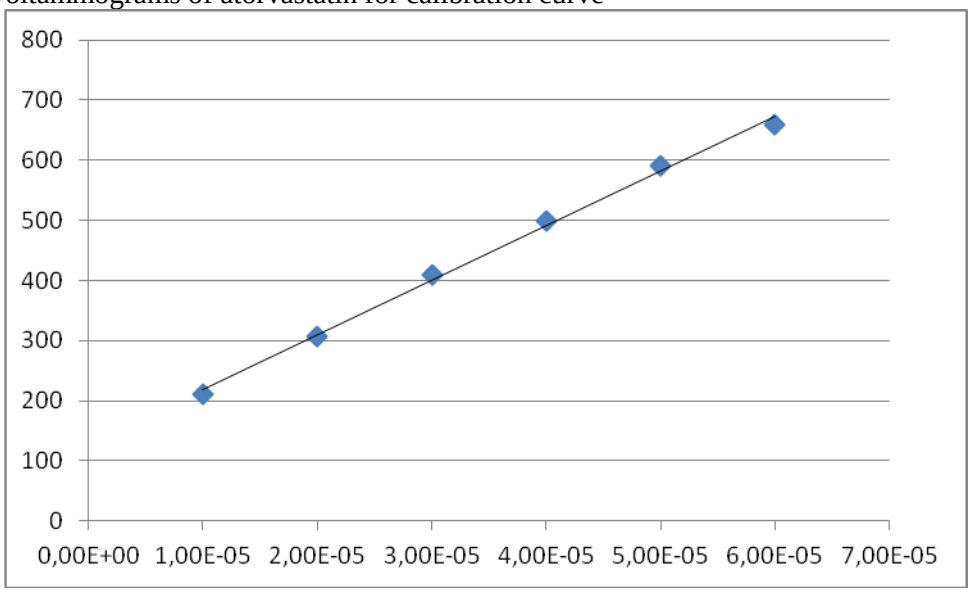


Figure 3. Linear relationship between CV signals and (ATOR) concentration over the range $1x10^{-5}$ – $6x10^{-5}$ mol L^{-1}

A last-square treatment of the calibration graph yielded the following regression equation:

$I(nA) = 9.1x10^{6} C + 127.73$ $r^2 = 0.998$ n = 6

Where I is the CV current, C is the analyzed drug concentration, r^2 is the correlation coefficient and n is number of measurements.

3.3.2. Repeatability and stability

The repeatability studies will be given more information about the analytical performance of the cyclic voltammetry method for determination of atorvastatin. In the analytical studies, the concentration $6x10^{-5}$ mol L^{-1} of atorvastatin was analyzed by CV. These voltammetric measurements were repeated ten times, yielded, relative standard deviation RSD

0.22 % (see table 1). On the other hand, the stability of the analytical CV signal was evaluated by monitoring the CV signal of atorvastatin for 90 minutes yielded, the CV currant approximately fixed within this analytical period.

Table 1. CV results of the repeatability study for the determination of Atorvastatin drug

ATOR concentration (mol L^{-1})	Current (nA)	(Average ± SD)	RSD(%)
6×10^{-5}	658	660.1 ± 1.45	0.22%
	660		
	659		
	661		
	662		
	662		
	660		
	661		
	660		
	658		

3.3.3. Detection limit

The detection limit, defined as three times the signal to noise ratio reached in the optimum conditions for monitoring this drug was 7.25×10^{-8} mol L^{-1} (0.04 ppm).

3.3.4. Analytical Applications

Cyclic voltammetric procedure applied to determine atorvastatin at pharmaceutical tablet. The cyclic voltammetric measurements were done by the standard addition method in order to minimize matrix effects. Five aliquots of this sample were analyzed by the proposed CV method. Atorvastatin content was analyzed directly using cyclic voltammetry (CV) method to be obtained electrochemical results as shown in the table 2.

Table 2. Analysis of Atorvastatin in commercial tablet (Lorvast 40 mg)

	Commercial tablet (Lorvast 40 mg)	
	Found conc (mol L^{-1})	Recovery %
Recovered ATOR Cone. 1×10^{-5} mol L^{-1}	1.9×10^{-5}	95.0%
	1.85×10^{-5}	92.5%
	1.95×10^{-5}	97.5%
	1.92×10^{-5}	96.0%
	1.94×10^{-5}	97.0%
Mean	96%	
Standard Deviation	±0.0198	

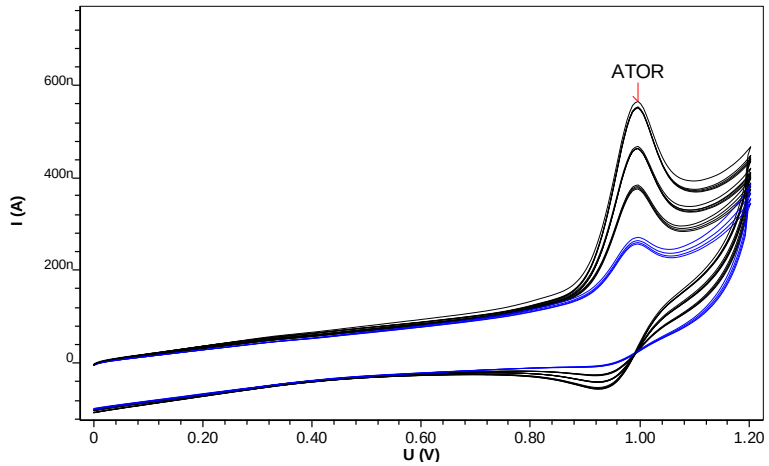


Figure 4. Cyclic voltammograms for the determination of atorvastatin in commercial tablet (Lorvast 40 mg) at phosphate buffer pH3 (five measurements for everyone)

4. Conclusion

Atorvastatin (ATOR) was determined by the developed cyclic voltammetry (CV) method in the presence of phosphate buffer pH3 under the selected parameters which given high and sharp CV signal. Calibration curve, detection limit, repeatability and stability were evaluated the analytical performance for CV method. Atorvastatin drug was determined at commercial pharmaceutical tablet "Lorvast 40 mg (manufactured by Tabuk pharmaceutical Mfg. Co. Tabuk-Saudi Arabia) in the local pharmacy. There are many published articles for the determination of ATOR using different analytical methods, but there is no anyone used GC electrode for the determination of ATOR.

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