

EFFECT OF HANGING MERCURY DROP ELECTRODE ON DIFFERENTIAL PULSE POLAROGRAPHIC ANALYSIS OF ATORVASTATIN IN PHARMACEUTICALS USING BORAX BUFFER AT pH7.50

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ABSTRACT

Using hanging mercury drop electrode (HMDE) for differential pulse polarographic analysis (DPPA) of atorvastatin (AT) in pure and pharmaceutical dosage forms in borax buffer at pH7.50 was developed. One reduction peak was observed in the range -1290 to -1330 mV (E_p). The peak current I_p is linear over the ranges 0.020-0.600 $\mu\text{mol.L}^{-1}$ (11.173-335.18ng.mL⁻¹); the sensitivity increased to about 100 times higher than using dropping mercury electrode (DME). The developed method has been used successfully for the determination of AT in pure form and in pharmaceuticals. The relative standard deviation did not exceed 3.5% for the concentrations of AT 0.020 $\mu\text{mol.L}^{-1}$ (11.173ng.mL⁻¹). Regression analysis showed a good correlation coefficient ($R^2=0.9995$) between I_p and concentration over the range of 11.173 to 335.18ng.mL⁻¹ with detection limit (LOD) and quantification limit (LOQ) of 1.29 and 3.89ng.mL⁻¹, respectively. The proposed method was successfully applied to the analysis of AT in pure and pharmaceutical dosage forms with average recovery of 97.2 to 104.2%. The results obtained agree well with the contents stated on the labels.

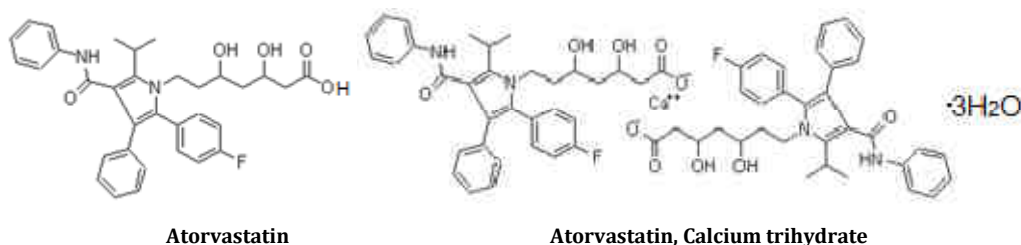
Keywords: Hanging mercury drop electrode, Differential Pulse Polarographic Analysis, Atorvastatin, Pharmaceuticals .

INTRODUCTION

Atorvastatin calcium^{1, 2} is a calcium (bR, dR)-2-(*r*-fluorophenyl)-b, d-dihydroxy-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)pyrrole-1-hepatanoic acid (1:2) trihydrate. The empirical formula of atorvastatin calcium trihydrate is $\text{C}_{66}\text{H}_{68}\text{CaF}_2\text{N}_4\text{O}_{10} \cdot 3\text{H}_2\text{O}$ or $(\text{C}_{33}\text{H}_{34}\text{FN}_2\text{O}_5)_2\text{Ca} \cdot 3\text{H}_2\text{O}$, mol. mass 1209.4 g; where the empirical formula of atorvastatin is $\text{C}_{33}\text{H}_{35}\text{FN}_2\text{O}_5$, mol. mass 558.64 g (Scheme1). Atorvastatin calcium is a white to off-white crystalline powder that is insoluble in aqueous solutions of pH 4 and below. Atorvastatin calcium is very slightly soluble in distilled water, pH 7.4 phosphate buffer, and acetonitrile; slightly soluble in ethanol; and

freely soluble in methanol. Atorvastatin is a member of the drug class known as statins, used for lowering blood cholesterol. It also stabilizes plaque and prevents strokes through anti-inflammatory and other mechanisms²⁻⁴.

Several studies have been reported for the determination of atorvastatin in pure form, in pharmaceutical formations and in biological fluids including spectrophotometric methods^{2, 5-10}, chromatographic methods with different detectors¹¹⁻²⁶ and electrochemical methods analysis²⁷⁻³³. The polarographic analysis was successfully applied for determination some drugs as gatifloxacin³⁴, Carbinoxamine Maleate³⁵, Dipyrone³⁶ and Lomefloxacin³⁷.



Scheme 1: Chemical structure of Atorvastatin and atorvastatin calcium trihydrate.

Atorvastatin was determined in pharmaceutical preparations and human plasma using differential pulse polarographic and square wave voltammetric techniques by reduction at a dropping-mercury working electrode versus Ag/AgCl reference electrode. Optimum conditions such as pH, scan rate, and pulse amplitude were studied, and validation of the proposed methods was performed. The proposed methods proved to be accurate, precise, robust and specific for determination of atorvastatin drug. The relative standard deviation values were <2%. Limits of detection and quantitation were 0.21 and 0.71 $\mu\text{g/mL}$, respectively²⁹.

A capillary electrophoretic method for the rapid quantitation of atorvastatin (AT) in a tablet was investigated and developed. Optimum conditions such as applied potential, buffer concentration, buffer pH, and hydrodynamic injection time on the electrophoretic separation were studied. The method was validated with regard to linearity, precision, specificity, LOD, and LOQ. Analysis of AT in a commercial tablet by electrophoresis gave quite high efficiency, coupled with an analysis time of less than 1.2 min in comparison to LC. This work represents the most rapid and first reported analysis of AT using microchip electrophoresis (MCE)²⁸.

The property was exploited in developing a highly sensitive stripping voltammetric procedure for the determination of the atorvastatin drug. The anodic current of adsorbed compound is measured by differential pulse and Osteryoung square wave adsorptive stripping voltammetry, preceded by a period of preconcentration. The effect of various parameters such as supporting electrolyte composition, pH, initial potential, scan rate, accumulation time, and ionic strength are discussed. The methods were performed in Britton-Robinson buffer, and the corresponding calibration graphs were constructed and statistical parameters evaluated. Applying the differential pulse adsorptive stripping voltammetry and Osteryoung square wave adsorptive stripping voltammetric method at pH 2.0 linearity was achieved from 3.5×10^{-8} to 4.6×10^{-7} M for square wave adsorptive stripping voltammetry with limit detection and limit quantitation of 4.0×10^{-9} M, 2.0×10^{-9} M and 1.0×10^{-8} M, 2.0×10^{-8} M, respectively. Since the proposed methods enabled lower concentrations of atorvastatin to be determined, this method was tested for atorvastatin determination in pharmaceutical products and spiked human plasma³⁰.

Novel differential pulse polarographic analysis (DPPA) by using dropping mercury electrode (DME) with negative amplitude was applied for determination of atorvastatin (AT) in pure and pharmaceutical dosage forms in borax buffer at pH 7.5. One reduction peak was observed in the range -1310 to -1340 mV (E_p). The peak current I_p is linear over the ranges 2.00-60.00 $\mu\text{mol.L}^{-1}$. The DPPA has been used successfully for the determination of AT in pure form and in pharmaceutical formulations. The relative standard deviation did not exceed 3.8% for the concentrations of AT 2.00 $\mu\text{mol.L}^{-1}$ (1.117 $\mu\text{g.mL}^{-1}$). Regression analysis showed a good correlation coefficient ($R^2 = 0.9994$) between I_p and concentration over the range of 1.117 to 33.52 $\mu\text{g.mL}^{-1}$. The limit of detection (LOD) and the limit of quantification (LOQ) were to be 0.129 $\mu\text{g.mL}^{-1}$ and 0.390 $\mu\text{g.mL}^{-1}$, respectively. The proposed method was successfully applied to the analysis of AT in pure and pharmaceutical dosage forms with average recovery of 97.2 to 104.2%. The results obtained agree well with the contents stated on the labels³³.

In the present work, differential pulse polarographic analysis (DPPA) on hanging mercury drop electrode (HMDE) with negative amplitude was applied for determination of atorvastatin in pure form and in pharmaceutical dosage forms using borax buffer at pH 7.5.

MATERIALS AND METHODS

Reagents

Sodium tetraboratedecahydrate (borax, $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$), methanol and phosphoric acid, were purchased from Merck. Atorvastatin Calcium trihydrate was supplied by ind-swift (India), its purity as atorvastatin was 92.0%. Supporting electrolyte of 0.075 mol.L^{-1} and 0.013 mol.L^{-1} of $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ and H_3PO_4 was prepared by dissolving 28.5 g of $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ in 900 mL double distilled deionized water then adding 26 mL of H_3PO_4 (1.0 M) and completing to 1000 mL in volumetric flask by adding double distilled deionized water (pH=7.5). A stock standard solutions of atorvastatin calcium trihydrate 1×10^{-5} mol.L^{-1} of atorvastatin was prepared by dissolving 30.36 mg from atorvastatin calcium trihydrate in 50 mL mixture methanol:water (9:1, v/v) 1×10^{-3} mol.L^{-1} then dilute 1.00 mL from this solution to 100 mL (1×10^{-5} mol.L^{-1}). The stock solution was further diluted to obtain working solutions daily just before use in the ranges of atorvastatin: 0.020, 0.040, 0.060, 0.080, 0.100, 0.120, 0.160, 0.200, 0.300, 0.400, 0.500 and 0.600 $\mu\text{mol.L}^{-1}$ (11.17, 22.34, 33.52, 44.69, 55.86, 67.04, 89.38, 111.73, 167.59, 223.40, 279.32 and 335.18 ng.mL^{-1}) by dilution of the volumes: 0.050, 0.100, 0.150, 0.200, 0.250, 0.300, 0.400, 0.500, 0.750, 1.000, 1.250 and 1.500 mL from stock standard solutions to 25 mL with supporting electrolyte. All solutions and reagents were prepared with double-distilled deionised water and analytical grade chemicals. Ultrapure mercury from Metrohm Company was used throughout the experiments.

Instruments and apparatus

A Metrohm 746 VA processor, A Metrohm 747 VA stand with a hanging mercury drop electrode (HMDE) as a working electrode, where the HMDE instruction is used to form mercury drops through a glass capillary electrode of defined size and the last drop remains suspended and thus forms the hanging mercury drop electrode at which a voltage sweep can be performed, an auxiliary platinum electrode and a reference electrode, double junction type, (Ag/AgCl) saturated with a 3.0 M KCl solution and the three-electrode cell were used. All measurements were done at room temperature 25 ± 5 °C. Highly pure nitrogen gas (99.999 %) was used for de-oxygenation. pH meter from Radio meter company model ion check was used for the studying and monitoring the pH effects. The diluter pipette model DIP-1 (Shimadzu), having 100 μL sample syringe and five continuously adjustable pipettes covering a volume range from 20 to 5000 μL (model PIPMAN P, GILSON), were used for preparation of the experimental solutions. A ultrasonic processor model POWERSONIC 405 was used to sonicate the sample solutions. Electronic balance (Sartorius-2474; $d=0.01$ mg) was used for weighing the samples.

Sample preparation

A commercial formulations (as tablet) were used for the analysis of atorvastatin (AT) by using DPPA with HMDE. The pharmaceutical formulations were subjected to the analytical procedures:

- (1) **Atorvex** tablets, Asia pharmaceutical industries, Aleppo-SYRIA, each tablet contains: 10, 20 and 40 mg of AT.
- (2) **Atorvatin** tablets, Alpha, Aleppo pharmaceutical industries, Aleppo-SYRIA, Each tablet contains: 10, 20 and 40 mg of AT.
- (3) **Lipito-med** tablets, Medico labs., Homs-SYRIA, Each tablet contains: 10, 20 and 40 mg of AT.
- (4) **Lipostatin** tablets, Ibn Al-Haytham Pharma Industries Co., Aleppo-SYRIA, each tablet contains: 10, 20 and 40 mg of AT.
- (5) **Atoraz** tablets, Razi pharmaceutical industries, Aleppo-SYRIA, each tablet contains: 10, 20 and 40 mg of AT.

Stock solutions of pharmaceutical formulations

Three tablets of each studied pharmaceutical formulations were weighted accurately, crushed to a fine powder and mixed well. Equivalent tenth the weight of one tablet, was solved in 20 mL methanol:water (9:1) by using ultrasonic, filtered over a 50 mL flask and diluting to 50 mL with methanol:water, which content as the follows: 20, 40 and 80 $\mu\text{g.mL}^{-1}$ then dilute 1.00 mL from this solution to 100 mL (400, 800 and 1600 ng.mL^{-1}) for all studied pharmaceutical formulations content 10, 20 and 40 mg/tab, respectively.

Working solutions of pharmaceuticals

These solutions were prepared daily by diluting 3.125, 1.562 and 0.781 mL from stock solutions of pharmaceutical formulations, respectively, then diluting to 25 mL with supporting electrolyte (each solution contents 50.0 ng.mL^{-1} of atorvastatin).

Working standard addition solutions of pharmaceuticals

These solutions were prepared as the follows: same mentioned volumes of stock solutions of pharmaceuticals with 0.224, 0.448, 0.671 and 0.895 mL from stock solution of atorvastatin and diluting to 25 mL with supporting electrolytes; these solutions content 50.0 ng.mL^{-1} of AT (for different pharmaceuticals) plus 50.0, 100.0, 150.0 and 200.0 ng.mL^{-1} of AT, respectively.

Analytical procedure

25 mL of working standard of atorvastatin was transferred to the cell. The solution was well mixed by automatic mixer and deoxygenated with nitrogen gas for 100s. Current-voltage curves were recorded. Limiting currents were measured and calibration curves in electrolytes were constructed.

RESULTS AND DISCUSSION

Polarographic behaviour

The polarograms in the optimal conditions (supporting electrolytes, pH, scan rate, initial potential and final potential, etc.) using DPPA at HMDE were studied. The peak potential was measured at -1290 to -1330 mV.

The effect of pH

The influence of pH on I_p was studied. The maximum peak (I_p) occurs at approximately pH 7.5, see Figure 1. The effect of pH on peak potential (E_p) shows the following: when pH value decreasing between 9 to 6.5, E_p remains almost constant, but decreases pH value after that E_p increases sharply to negative value.

The effect of supporting electrolytes (buffer)

The effect of supporting electrolytes (buffer) on the I_p was studied. It was found that, the borax was the better buffer at concentration 0.075 mol.L^{-1} .

The effect of negative pulse amplitude

The effect of negative pulse amplitude between 0 to 100 mV on I_p showed that, the value 100 mV was better than another's.

The effect of scan rate

The different values of scan rate (4, 8, 12, 16, 20 and 24mV/s) were studied. It was found that, the value scan rate 12 mV/s was the better.

The effect of initial and final potential

The effect of initial and final potential on the I_p was studied. It was found that better initial potential was -900 mV and better final potential was -1500 mV.

The effect of temperature and time

The effect of temperature and time on the electrochemical reaction of atorvastatin was studied at different values (15-35°C, 5-60 min) by continuous monitoring of the I_p . It was found that, the value of I_p was not affected by temperature between 20 to 30 (the temperature at 25±5°C was used). The effect of waiting time was determined at laboratory ambient temperature (25±5°C). It was found that, the value of I_p was not affected by time between 5 to 60 min.

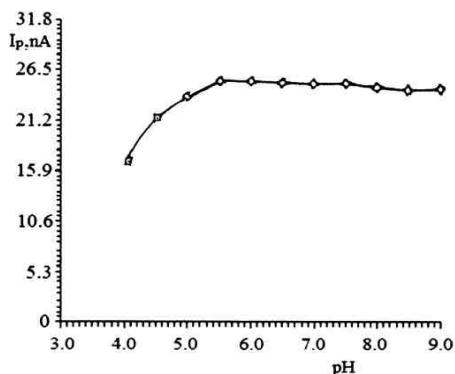


Fig. 1: The effect of pH solution on I_p of atorvastatin using DPPA at HMDE in borax buffer, (C_{AT} = 76.0 ng.mL⁻¹).

The effect of time pulse (t. pulse): The effect of time pulse on polarograms was as the follows: I_p decreases with increasing time pulse. E_p has become increasingly latency positive value (-1321 to -1289 mV) with increasing t. pulse. The peak was more symmetrical when the pulse value of 33ms.

The effect of voltage step (U. step): I_p increases with increasing U. step to value 10mV then was constant. E_p has become increasingly latency negative value (-1303 to -1315 mV) with increasing U. step. The value of the preferred U. Step was 6 mV.

The effect of voltage time step (t. step): I_p increases with increasing t. step to value 0.5s then was approximately constant. E_p has become increasingly latency positive value (-1300 to -1278 mV) with increasing t. step. The value of the preferred t. Step was 0.5 s.

The effect of measurement time (t. meas.): I_p increases with increasing t. meas. from 1 to 8 ms then was constant until 24 ms and after that increases. E_p has become increasingly latency negative value (-1298 to -1307 mV) with increasing t. meas. The value of the preferred t. Meas. was 20ms.

The effect of drop size: I_p increases with increasing drop size from 1 to 9 size. E_p has become proximal constant -1294 to -1296 mV) with increasing drop size. The value of the preferred drop size was 9.

The effect of measurement voltage (U. meas.): Initially I_p sharply increases with increasing U. meas. from 0 to 200 mV then after that was approximately constant. E_p has become increasingly latency negative value (-1290 to -1302 mV) with increasing U. meas. From -200 to -600 mV, see Figure 2. The value of the preferred U. meas. was -300 mV.

The optimum parameters established for determination of AT using DPPA on HMDE showed in Table 1.

Calibration curves: Calibration curves for the determination of atorvastatin using differential pulse polarographic analysis on hanging mercury drop electrode with negative amplitude in borax buffer at pH 7.5 were applied. The peak current (I_p) was proportional to the concentration of AT over the ranges 0.020-0.600 $\mu\text{mol.L}^{-1}$ (11.17-335.18ng.mL⁻¹). The polarograms in the optimum conditions using DPPA at HMDE of AT at different concentrations show in Figure 3. The regression equation and correlation coefficient (R^2) were as the follows: $y=0.3306x+0.1912$, $R^2=0.9995$; y: I_p , nA and x: C_{AT} , ng.mL⁻¹, see Figure 4.

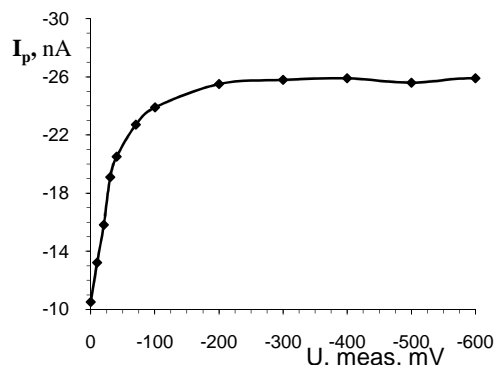


Fig. 2: The effect of measurement voltage (U. meas.) on I_p of atorvastatin using DPPA at HMDE in borax buffer, pH7.5 (C_{AT} = 76.0 ng.mL⁻¹).

Table 1: The optimum parameters established for determination of atorvastatin using differential pulse polarographic analysis on hanging mercury drop electrode (HMDE) with negative amplitude in borax buffer at pH 7.5

Parameters	Operating modes
Working electrode	Hanging mercury drop electrode (HMDE)
Supporting electrolyte (buffer)	Borax, 0.075 mol.L ⁻¹
pH	7.5
Solvent for atorvastatin	Methanol:water (9:1, v/v)
Value of pulse amplitude	-100 mV
Purge gas	Pure N ₂
Purge time	100 s
Initial potential	-900 mV
Final potential	-1500 mV
Pulse duration	20 ms
Scan rate	12 mV/s
U. meas.	-300 mV
U. amplitude	-100 mV
U. step	6 mV
Drop size	9
t. meas.	20 ms
t. pulse	33 ms
t. step	0.5 s
Temperature of solution	25± 5°C
Peak Potential, mV	-1290 to -1330 mV
LOD(3.3SD)	1.29ng.mL ⁻¹
LOQ (10SD)	3.98ng.mL ⁻¹
Linearity range of concentration	11.173ng.mL ⁻¹ (0.020 μM) to 335.18ng.mL ⁻¹ (0.600 μM)
Regression equation:	* $y=0.3306x+0.1912$
Slope	0.3306
Intercept	0.050
Correlation coefficient (R^2)	0.9995
RSD	3.5%

* y= nA, x= concentration of atorvastatin (ng.mL⁻¹).

Analytical results

Determination of atorvastatin using differential pulse polarographic analysis on hanging mercury drop electrode (HMDE) with negative amplitude in borax buffer at pH 7.5 using analytical curves, $I_p=f(C_{AT})$, showed that the accuracy was ready over the ranges of AT

concentration between 11.17–335.18ng.mL⁻¹; the sensitivity increased to about 100 times higher than when using the dropping mercury electrode (DME)³³. The relative standard deviation (RSD) not more than 3.5%, see Table 2. Limit of detection (LOD) and limit of quantitation (LOQ) for the determination of AT by this method were as the follows : 1.29 and 3.98ng.mL⁻¹, respectively.

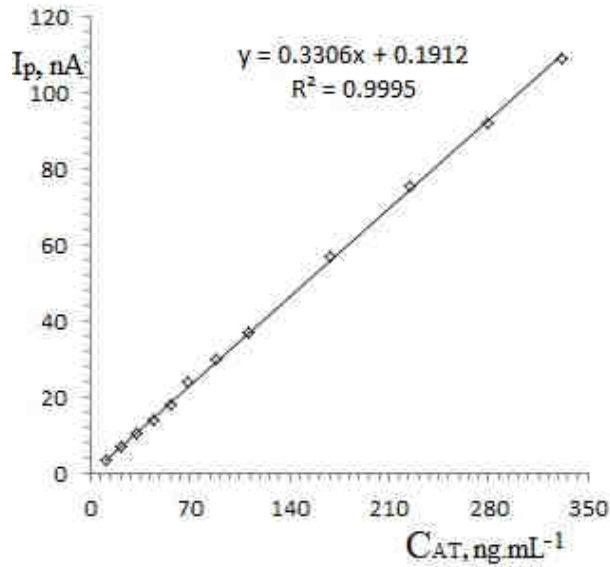


Fig. 3: The polarograms in the optimum conditions using DPPA at HMDE of AT at concentrations: 1- 0; 2- 11.17; 3- 22.34;4- 33.52; 5- 44.69; 6- 55.86; 7- 67.04;8- 89.38; 9- 111.73; 10- 167.59; 11- 223.40;12- 279.32 and 13- 335.18ng.mL⁻¹.

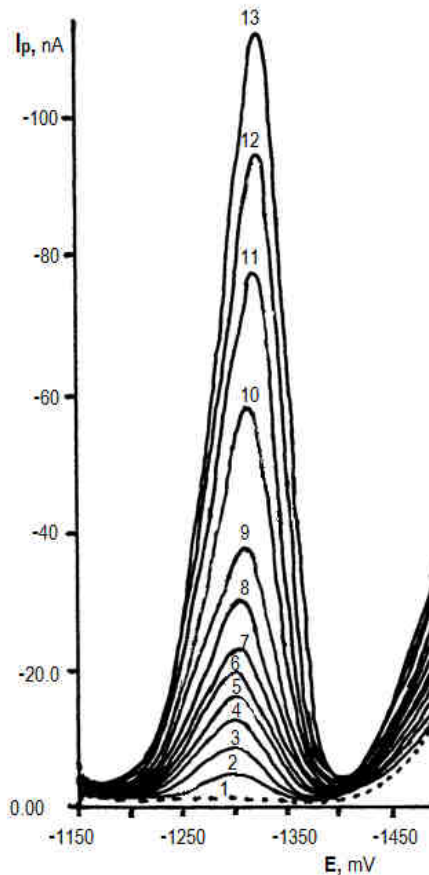


Fig. 4: Calibration curves for the determination of atorvastatin using differential pulse polarographic analysis on hanging mercury drop electrode with negative amplitude in borax buffer at pH 7.5.

Table 2: Determination of atorvastatin using differential pulse polarographic analysis on hanging mercury drop electrode(HMDE)with negative amplitude in borax buffer at pH 7.5

$x_i, \text{ng.mL}^{-1}$ (Taken)	$\bar{x}^*, \text{ng.mL}^{-1}$ (Found)	SD, ng.mL^{-1}	$\frac{SD}{\sqrt{n}}$, ng.mL^{-1}	$\bar{x} \pm \frac{t \cdot SD}{\sqrt{n}}$, ng.mL^{-1}	RSD %
11.17	10.9	0.38	0.17	10.9± 0.47	3.5
22.34	21.9	0.74	0.33	21.9± 0.91	3.4
33.52	32.9	1.09	0.49	32.9± 1.4	3.3
44.69	44.5	1.47	0.66	44.5± 1.8	3.3
55.89	55.8	1.78	0.80	55.8± 2.2	3.2
67.04	69.2	2.14	0.96	69.2± 2.7	3.1
89.38	89.0	2.67	1.16	89.0± 3.2	3.0
111.73	111.7	3.24	1.45	111.7± 4.0	2.9
167.59	168.1	4.71	2.11	168.1± 5.8	2.8
223.40	225.0	6.30	2.82	225.0± 7.8	2.8
279.32	279.1	7.53	3.37	279.1± 9.3	2.7
335.18	332.3	8.64	3.86	332.3± 10.7	2.6

* n=5, t=2.776.

Applications

Many applications for the determination of atorvastatin in some Syrian pharmaceutical preparations using differential pulse polarographic analysis on hanging mercury drop electrode with negative amplitude in borax buffer at pH 7.5 were proposed. Standard addition curves for determination of AT in different Syrian pharmaceutical preparations (*Atorvex*, *Atorvatin*, *Lipito-med*, *Lipostat* and *Atoraz*) were used. The standard addition curve of *Atorvex* (10 mg/tab.) was showed in Fig. 5, as an example. Regression equations and correlation coefficients were included in Table 3. Standard addition curves for determination of AT in different Syrian pharmaceutical preparations were used. The

amount (m) of AT in one tablet by mg/tab ($m_{AT}/\text{tab.}$) calculated from the following relationship: $m = h \cdot m'$, where: m' is the amount of AT in tablet, which calculated from the standard additions curve according to the following regression equation: $y = a \cdot x + b$; when $y = 0$; $m' = -x \cdot b/a = \text{intercept/slope (ng.mL}^{-1}\text{)}$ and h conversion factor is equal to 0.20, 0.40 and 0.80 for all pharmaceuticals content 10, 20 and 40 mg/tab, respectively.

The results of quantitative analysis for AT in the pharmaceutical preparations using this method were included in Tables 4. The proposed method was simple, economic, accurate and successfully applied to the determination of atorvastatin in pharmaceuticals. The results obtained agree well with the contents stated on the labels.

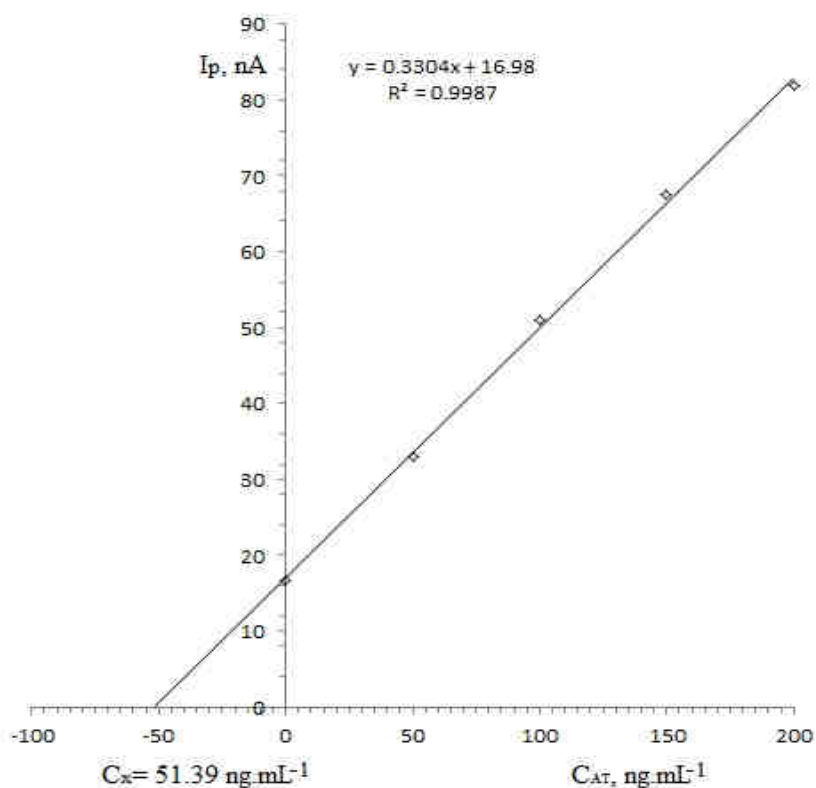


Fig. 5: The standard addition curve for determination of atorvastatin in *Atorvex* (10 mg/tab.) using differential pulse polarographic analysis on hanging mercury drop electrode with negative amplitude in borax buffer at pH 7.5.

Table 3: Regression equations and correlation coefficients for determination of atorvastatin in Syrian pharmaceutical preparations using differential pulse polarographic analysis on HMDE with negative amplitude in borax buffer at pH 7.5

Pharmaceutical preparations	Atorvastatin In tab., mg	Operating modes		
		Regression equations*	Correlation coefficients	Amount of atorvastatin (m), mg/tab.
Atorvex , Ctd. tab.	10	y=0.3304x+16.98	R ² =0.9987	m _{AT/tab.} =0.20m'=10.28
Asia pharmaceutical industries	20	y=0.3304x+17.21	R ² =0.9987	m _{AT/tab.} =0.40m'=20.85
Aleppo-SYRIA	40	y=0.3305x+16.94	R ² =0.9991	m _{AT/tab.} =0.80m'=41.00
Atorvatin , Ctd. tab.	10	y=0.3306x+16.20	R ² =0.9983	m _{AT/tab.} =0.20m'=9.80
Alpha Aleppo Pharmaceutical Industries - SYRIA	20	y=0.3307x+16.58	R ² =0.9984	m _{AT/tab.} =0.40m'=20.06
40	y=0.3305x+16.12	R ² =0.9985	m _{AT/tab.} =0.80m'=39.01	
Lipito-med , Ctd. tab.	10	y=0.3308x+16.44	R ² =0.9987	m _{AT/tab.} =0.20m'=9.94
Medico Labs. Homs-SYRIA	20	y=0.3307x+16.73	R ² =0.9987	m _{AT/tab.} =0.40m'=20.24
40	y=0.3306x+16.58	R ² =0.9988	m _{AT/tab.} =0.80m'=40.12	
Liostatin , Ctd. tab.	10	y=0.3305x+17.02	R ² =0.9982	m _{AT/tab.} =0.20m'=10.30
Ibn Ai Haytham , Pharma Industries Co. Aleppo-SYRIA	20	y=0.3308x+16.84	R ² =0.9985	m _{AT/tab.} =0.40m'=20.36
40	y=0.3307x+16.73	R ² =0.9990	m _{AT/tab.} =0.80m'=40.48	
Atoraz , Ctd. tab.	10	y=0.3306x+16.10	R ² =0.9982	m _{AT/tab.} =0.20m'=9.74
Razi pharmaceutical industries Aleppo-SYRIA	20	y=0.3307x+16.45	R ² =0.9986	m _{AT/tab.} =0.40m'=19.90
40	y=0.3306x+16.60	R ² =0.9989	m _{AT/tab.} =0.80m'=40.16	

*y= n A, x= concentration of atorvastatin (ng.mL⁻¹)= m' = intercept/slope.

Table 4: Determination of atorvastatin in Syrian pharmaceutical preparations using differential pulse polarographic analysis on HMDE with negative amplitude in borax buffer at pH 7.5

Commercial name	Contents, mg/tab.	* \bar{X} , mg/tab.	RSD%	Recovery %
Atorvex , Ctd. tab.	10	10.28	3.6	102.8
Asia pharmaceutical industries	20	20.85	3.5	104.3
Aleppo-SYRIA	40	41.00	3.4	102.5
Atorvatin , Ctd. tab.	10	9.80	3.7	98.0
Alpha , Aleppo Pharmaceutical Industries	20	20.06	3.6	100.3
Aleppo-SYRIA	40	39.01	3.4	97.5
Lipito-med , Ctd. tab.	10	9.94	3.7	99.4
Medico Labs. Homs-SYRIA	20	20.24	3.5	101.2
40	40.12	3.4	100.3	
Liostatin , Ctd. tab.	10	10.30	3.6	103.0
Ibn Al Haytham, Pharma Industries Co. Aleppo-SYRIA	20	20.36	3.5	101.8
40	40.48	3.4	101.2	
Atoraz , Ctd. tab.	10	9.74	3.8	97.4
Razi pharmaceutical industries Aleppo-SYRIA	20	19.90	3.6	99.5
40	40.16	3.5	100.4	

*n=5

CONCLUSION

Using hanging mercury drop electrode (HMDE) for differential pulse polarographic analysis (DPPA) of atorvastatin (AT) in pure and pharmaceutical dosage forms in borax buffer at pH 7.50 was caused increasing the sensitivity about 100 times higher than using dropping mercury electrode. The reduction peak current I_p is linear over the ranges 0.020-0.600 $\mu\text{mol.L}^{-1}$ (11.173-335.18 ng.mL^{-1}). The developed method has been used successfully for the determination of AT in pure form and in pharmaceuticals. The limit of detection (LOD) and the limit of quantification (LOQ) were to be 1.29 ng.mL^{-1} and 3.89 ng.mL^{-1} , respectively. The proposed method was successfully applied to the analysis of AT in pure and pharmaceutical dosage forms with average recovery of 97.2 to 104.2%. The results obtained agree well with the contents stated on the labels.

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