

DIFFERENTIAL PULSE POLAROGRAPHY OF ATORVASTATIN IN PURE AND PHARMACEUTICAL DOSAGE FORMS USING STATIC MERCURY DROP ELECTRODE

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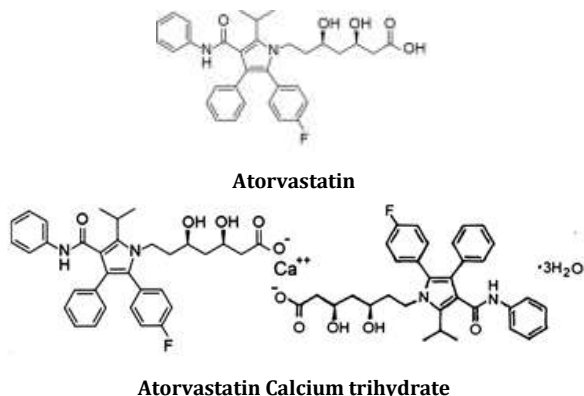
ABSTRACT

The differential pulse polarography (DPP) of atorvastatin (AT) in pure and pharmaceutical dosage forms in borax buffer media has been investigated using static mercury drop electrode (SMDE). One reduction peak was observed in the range -1340 to -1385 mV (E_p). The peak current I_p is linear over the ranges 0.2234-24.580 $\mu\text{g}\cdot\text{mL}^{-1}$; the sensitivity increased to about 5 times higher than using dropping mercury electrode (DME). The relative standard deviation did not exceed 3.2% for the concentrations of AT 0.2234 $\mu\text{g}\cdot\text{mL}^{-1}$. Regression analysis showed a good correlation coefficient ($R^2=0.9999$) between I_p and concentration over the studied range with detection limit (LOD) and quantification limit (LOQ) of 0.024 and 0.071 $\mu\text{g}\cdot\text{mL}^{-1}$, respectively. The proposed method was successfully applied to the analysis of AT in pure and pharmaceutical dosage forms with average recovery of 97.0 to 105.0%. The results obtained agree well with the contents stated on the labels.

Keywords: Static mercury drop electrode, Differential Pulse Polarography, 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-heptanoic 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 (Scheme). Atorvastatin is a member of the drug class known as statins, used for lowering blood cholesterol²⁻⁴. Several studies have been reported for the determination of atorvastatin in pure form, in pharmaceutical formations and in biological fluids including spectrophotometric methods²⁻⁵,



Scheme: Chemical structure of Atorvastatin and atorvastatin calcium trihydrate

Chromatographic methods with different detectors⁵⁻⁸ and electrochemical methods analysis⁹⁻²¹. The polarographic analysis was successfully applied for determination some drugs as gatifloxacin¹⁶, Carbinoxamine Maleate¹⁷, Dipyrone¹⁸, Lomefloxacin¹⁹ and atorvastatin^{15, 21}.

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. 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 $\mu\text{g}/\text{mL}$, respectively²⁰.

The property was exploited in developing a highly sensitive stripping voltammetric procedure for the determination of the

atorvastatin drug. The methods were performed in Britton-Robinson buffer at pH 2.0, and the calibration graphs linearity were 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. This method was tested for atorvastatin determination in pharmaceutical products and spiked human plasma¹².

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. The peak current I_p is linear over the ranges 2.00-60.00 $\mu\text{mol}\cdot\text{L}^{-1}$. The relative standard deviation did not exceed 3.8%. Regression analysis showed a good correlation coefficient ($R^2=0.9994$). The limit of detection (LOD) and the limit of quantification (LOQ) were to be 0.129 $\mu\text{g}\cdot\text{mL}^{-1}$ and 0.390 $\mu\text{g}\cdot\text{mL}^{-1}$, 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 labels¹⁵.

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 exploited. 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 $\mu\text{mol}\cdot\text{L}^{-1}$ (11.173-335.18 $\text{ng}\cdot\text{mL}^{-1}$); 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 $\mu\text{mol}\cdot\text{L}^{-1}$ (11.173 $\text{ng}\cdot\text{mL}^{-1}$). Regression analysis showed a good correlation coefficient ($R^2=0.9995$) between I_p and concentration over the range of 11.173 to 335.18 $\text{ng}\cdot\text{mL}^{-1}$ with detection limit (LOD) and quantification limit (LOQ) of 1.29 and 3.89 $\text{ng}\cdot\text{mL}^{-1}$, 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 labels²¹.

The latest static mercury drop electrode (SMDE) combines the features of the mercury drop electrode (DME) and the hanging mercury drop electrode (HMDE): during the measurement, the drop surface is constant and stationary (as with the HMDE); however, for the complete voltage sweep several drops are needed (renewal as with the DME). A disadvantage of the DME compared with the SMDE and HMDE is the higher mercury consumption and the lower sensitivity as the electrode surface and hence the baseline constantly changes during the measurement phase. The SMDE is

primarily used for sensitive measurements in which the surface of the mercury drop must be renewed for every measurement²².

In the present work, the differential pulse polarography (DPP) of atorvastatin (AT) in pure and pharmaceutical dosage forms in borax buffer media has been investigated using static mercury drop working electrode (SMDE) versus Ag/AgCl reference electrode with negative amplitude.

MATERIALS AND METHODS

Instruments and apparatus

A Metrohm 746 VA processor, A Metrohm 747 VA stand with a static mercury drop electrode (SMDE) as a working electrode, mercury drop electrode (DME) and hanging mercury drop electrode (HMDE), 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 μ L sample syringe and five continuously adjustable pipettes covering a volume range from 20 to 5000 μ L (model PIPTMAN 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.

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 0.026 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 $5 \times 10^{-4} \text{ mol.L}^{-1}$ of atorvastatin was prepared by dissolving 15.18 mg from atorvastatin calcium trihydrate in 50 mL mixture methanol:water (9:1, v/v). The stock solution was further diluted to obtain working solutions daily just before use in the ranges of atorvastatin: 0.40, 1.00, 2.00, 3.00, 4.00, 6.00, 8.00, 10.00, 12.00, 16.00, 20.00, 24.00, 28.00, 32.00, 36.00, 40.00 and 44.00 $\mu\text{mol.L}^{-1}$ (0.2234, 0.5586, 1.1172, 1.675, 2.234, 3.352, 4.469, 5.586, 6.703, 8.937, 11.172, 13.406, 15.640, 17.875, 20.104, 22.345 and $24.580 \mu\text{g.mL}^{-1}$) by dilution of the necessary aliquots volumes from stock standard solutions of atorvastatin 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.

Sample preparation

A commercial formulations (as tablet) were used for the analysis of atorvastatin (AT) by using DPP with static mercury drop electrode (SMDE). 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 $\mu\text{g.mL}^{-1}$ for all studied pharmaceutical formulations content 10, 20 and 40 mg/tab, respectively.

Working solutions of pharmaceuticals

These solutions were prepared daily by diluting 2.500, 1.250 and 0.625 mL from stock solutions of pharmaceutical formulations, respectively, then diluting to 25 mL with supporting electrolyte (each solution contents $2.000 \mu\text{g.mL}^{-1}$ of atorvastatin).

Working standard addition solutions of pharmaceuticals

These solutions were prepared as the follows: same mentioned volumes of stock solutions of pharmaceuticals with 0.100, 0.200, 0.300 and 0.400 mL from stock solution of atorvastatin and diluting to 25 mL with supporting electrolytes; these solutions content $2.000 \mu\text{g.mL}^{-1}$ of AT (for different pharmaceuticals) plus 2.00, 4.000, 6.000 and $8.000 \mu\text{g.mL}^{-1}$ 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 200s. Current-voltage curves were recorded. Limiting currents were measured and calibration curves in electrolytes were constructed.

RESULTS AND DISCUSSION

Polarographic behavior

The polarograms in the optimal conditions (supporting electrolytes, pH, scan rate, initial potential and final potential etc.) using DPP at static mercury drop electrode (SMDE) were studied. The peak potential was measured at -1340 to -1385 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 and positive 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; however, the negative pulse amplitude was better than the same values of positive pulse amplitude in all case.

The effect of scan rate

The different values of scan rate (1.429, 2.857, 4.286, 5.714, 7.143 and 8.571 mV/s) were studied. It was found that, the value scan rate 5.714 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.

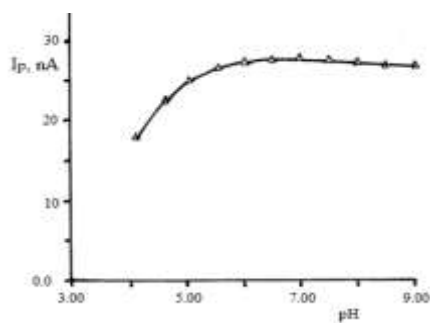


Fig. 1: The effect of pH solution on I_p of atorvastatin using DPP at static mercury drop electrode (SMDE) in borax buffer, ($C_{AT}=2.234 \mu\text{g.mL}^{-1}$).

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 (-1376 to -1341 mV) with increasing t. pulse. The peak was more symmetrical when the t. pulse value of 40ms.

The effect of voltage step (U. step): I_p increases with increasing U. step to value 8mV then was almost constant. E_p has become increasingly latency negative value (-1340 to -1385 mV) with increasing U. step. The value of the preferred U. Step was 8 mV.

The effect of voltage time step (t.step): I_p increases with increasing t. step to value 4s but the peak was more symmetrical at the t. step value 1.4s. E_p has become increasingly latency negative value (-1360 to -1375 mV) with increasing t. step. The value of the preferred t. step was 1.4 s.

The effect of measurement time (t.meas.): I_p increases with increasing t. meas. from 1 to 32ms. E_p has become increasingly latency negative value (-1350 to -1383 mV) with increasing t.meas. The value of the preferred t. meas. was 32ms.

The effect of drop size: I_p increases with increasing drop size from 1 to 9 size. E_p has become proximal constant (-1368 to -1372 mV) with increasing drop size. The value of the preferred drop size was 9.

The optimum parameters established for determination of AT using differential pulse polarography (DPP) in borax buffer media at static mercury drop electrode (SMDE) showed in Table 1.

Calibration curves

Calibration curves for the determination of atorvastatin using differential pulse polarography at static mercury drop electrode (SMDE) 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 $0.40\text{--}44.0 \mu\text{mol.L}^{-1}$ ($0.2234\text{--}24.580 \mu\text{g.mL}^{-1}$). The polarograms in the optimum conditions using DPP at SMDE of AT at different concentrations show in Figure 2. The regression equation and correlation coefficient (R^2) were as the follows: $y=12.616x+0.0217$, $R^2=0.9999$; y: I_p , nA and x: C_{AT} , $\mu\text{g.mL}^{-1}$, see Figure 3.

Table 1: The optimum parameters established for determination of atorvastatin using differential pulse polarography at static mercury drop electrode (SMDE) with negative amplitude in borax buffer at pH 7.5

Parameters	Operating modes
Working electrode	Static mercury drop working electrode(SMDE)
Supporting electrolytes (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	200 s
Initial potential	-900 mV
Final potential	-1500 mV
Scan rate	5.714 mV/s
U. amplitude	-100 mV
U. step	8 mV
Drop size	9
t. meas.	32ms
t. pulse	40ms
t. step	1.4 s
Temperature of solution	$25 \pm 5^\circ\text{C}$
Peak Potential, mV	-1340 to -1385 mV
LOD(3.3SD)	$0.024 \mu\text{g.mL}^{-1}$
LOQ (10SD)	$0.071 \mu\text{g.mL}^{-1}$
Linearity range of concentration	$0.2234 \mu\text{g.mL}^{-1}$ ($0.40 \mu\text{M}$) to $24.580 \mu\text{g.mL}^{-1}$ ($44 \mu\text{M}$)
Regression equation:	$*y=12.616x+0.0217$
Slope	12.616
Intercept	0.0217
Correlation coefficient (R^2)	0.9999
RSD	3.2%

* $y= \text{nA}$, $x= \text{concentration of atorvastatin (ng.mL}^{-1}\text{)}$.

Analytical results

Determination of atorvastatin using differential pulse polarography at static mercury drop electrode (SMDE) 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 $0.2234\text{--}24.580 \mu\text{g.mL}^{-1}$; the sensitivity increased to about 5 times higher than when using the dropping mercury electrode (DME)¹⁵. The relative standard deviation (RSD) not more than 3.2%, see Table 2. Limit of detection (LOD) and limit of quantitation (LOQ)

for the determination of AT by this method were as the follows : 0.031 and $0.094 \mu\text{g.mL}^{-1}$, respectively.

APPLICATIONS

Many applications for the determination of atorvastatin in some Syrian pharmaceutical preparations using differential pulse polarography at static mercury drop electrode (SMDE) with negative amplitude in borax buffer at pH 7.5 were proposed. Standard addition curves were used for determination of AT in different

Syrian pharmaceutical preparations (*Atorvex*, *Atorvatin*, *Lipito-med*, *Lipostatin* and *Atoraz*). The standard addition curve of *Lipito-med*, Ctd. tab. Medico Labs. Homs-SYRIA (10 mg/tab.) was showed in Fig. 4, 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 applied. 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: $y=a.x+b$; where: (a) is slope (ranging between 12.60-

12.63), (b) is Intercept (ranging between 24.425-25.997) and (y) is value of I_p (nA). When $y=0$; $m'=x= b/a= \text{intercept/slope } (\mu\text{g.mL}^{-1})$ and h conversion factor is equal to 5, 10 and 20 for all pharmaceuticals content 10, 20 and 40 mg/tab, respectively.

Regression analysis showed a good correlation coefficient (R^2 between 0.9993 - 0.9999). 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.

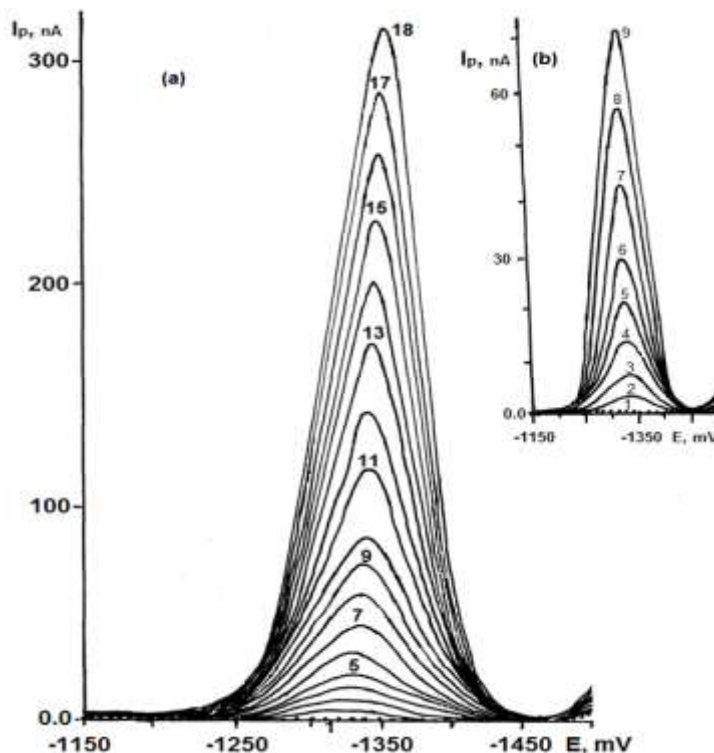


Fig. 2: The polarograms in the optimum conditions using DPP at static mercury drop electrode (SMDE) in borax buffer of AT at concentrations: 1- 0; 2- 0.2234; 3- 0.5586; 4- 1.1172; 5- 1.675; 6- 2.234; 7- 3.352; 8- 4.459; 9- 5.586; 10- 6.703; 11- 8.937; 12- 11.172; 13- 13.406; 14- 15.640; 15- 17.875; 16- 20.110; 17- 22.344 and 18- 24.580 $\mu\text{g.mL}^{-1}$.

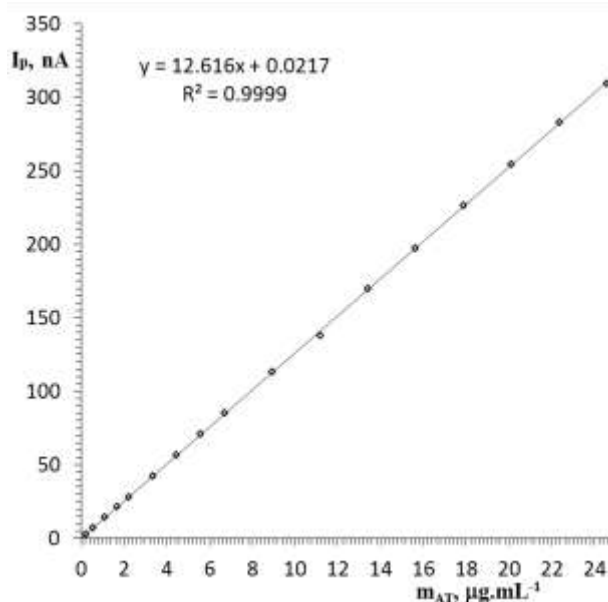


Fig. 3: Calibration curves for the determination of atorvastatin using differential pulse polarography static mercury drop electrode (SMDE) with negative amplitude in borax buffer at pH 7.5 .

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

$x_i, \mu\text{g.mL}^{-1}$ (Taken)	\bar{x}_1^* , $\mu\text{g.mL}^{-1}$ (Found)	Standard deviation SD, $\mu\text{g.mL}^{-1}$	Analytical standard error $\frac{SD}{\sqrt{n}}$, $\mu\text{g.mL}^{-1}$	Confidence limit $\bar{x} \pm \frac{t.SD}{\sqrt{n}}$, $\mu\text{g.mL}^{-1}$	RSD %
0.2234	0.228	0.0073	0.0032	0.228 ± 0.008	3.2
0.5586	0.559	0.018	0.0080	0.559 ± 0.022	3.2
1.1172	1.12	0.034	0.015	1.12 ± 0.042	3.1
1.6570	1.68	0.050	0.022	1.68 ± 0.061	3.0
2.2345	2.24	0.067	0.030	2.24 ± 0.083	3.0
3.3516	3.36	0.097	0.043	3.36 ± 0.12	2.9
4.469	4.48	0.125	0.056	4.48 ± 0.16	2.8
5.586	5.60	0.15	0.067	5.60 ± 0.19	2.7
6.703	6.74	0.17	0.076	6.74 ± 0.21	2.6
8.937	8.96	0.23	0.103	8.96 ± 0.29	2.5
11.172	10.94	0.26	0.116	10.94 ± 0.32	2.4
13.406	13.45	0.31	0.139	13.45 ± 0.38	2.3
15.640	15.61	0.33	0.148	15.61 ± 0.41	2.2
17.875	17.93	0.38	0.170	17.93 ± 0.47	2.1
20.110	20.17	0.42	0.188	20.17 ± 0.52	2.1
22.344	22.41	0.49	0.219	22.41 ± 0.61	2.2
24.580	24.49	0.59	0.264	24.49 ± 0.73	2.4

* n=5, t=2.776.

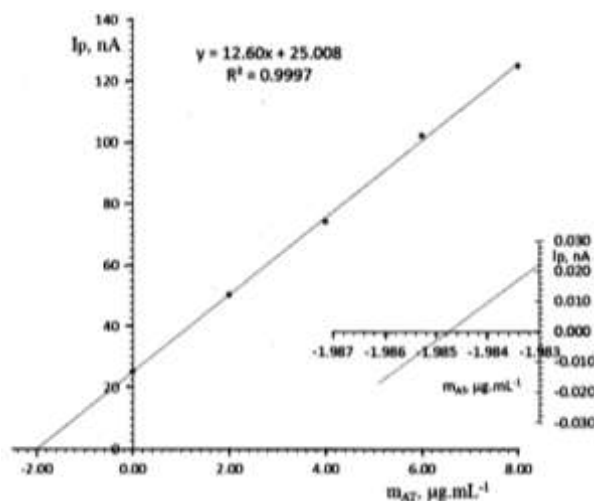


Fig. 4: The standard addition curve for determination of atorvastatin in *Lipito-med*, Ctd. tab., Medico Labs., Homs- SYRIA (10 mg/tab.) using differential pulse polarography at static mercury drop electrode (SMDE) with negative amplitude in borax buffer at pH 7.5 ($m' = 1.9848 \approx 1.985$).

Table 3: Regression equations, correlation and (m') coefficients for determination of atorvastatin in Syrian pharmaceutical preparations using differential pulse polarography at SMDE with negative amplitude in borax buffer at pH 7.5

Pharmaceutical preparations	Atorvastatin In tab., mg	Operating modes		m' , $\mu\text{g.mL}^{-1}$	Amount of atorvastatin (m), mg/tab.
		Regression equations*	Correlation coefficients		
<i>Atorvex</i> , Ctd. tab.	10	$y = 12.60x + 25.326$	$R^2 = 0.9996$	2.010	$m_{AT/tab.} = 5m' = 10.05$
Asia pharmaceutical industries Aleppo-SYRIA	20	$y = 12.62x + 25.997$	$R^2 = 0.9997$	2.060	$m_{AT/tab.} = 10m' = 20.60$
	40	$y = 12.61x + 26.481$	$R^2 = 0.9996$	2.100	$m_{AT/tab.} = 20m' = 42.00$
<i>Atorvatin</i> , Ctd. tab.	10	$y = 12.59x + 24.425$	$R^2 = 0.9993$	1.940	$m_{AT/tab.} = 0.20m' = 9.70$
Alpha Aleppo Pharmaceutical Industries SYRIA	20	$y = 12.60x + 24.948$	$R^2 = 0.9993$	1.983	$m_{AT/tab.} = 10m' = 19.80$
	40	$y = 12.62x + 24.998$	$R^2 = 0.9996$	1.981	$m_{AT/tab.} = 20m' = 39.60$
<i>Lipito-med</i> , Ctd. tab.	10	$y = 12.60x + 25.008$	$R^2 = 0.9997$	1.985	$m_{AT/tab.} = 0.20m' = 9.92$
Medico Labs. Homs-SYRIA	20	$y = 12.61x + 25.510$	$R^2 = 0.9997$	2.023	$m_{AT/tab.} = 10m' = 20.23$
	40	$y = 12.63x + 25.380$	$R^2 = 0.9998$	2.010	$m_{AT/tab.} = 20m' = 40.19$
<i>Liostatin</i> , Ctd. tab.	10	$y = 12.61x + 25.478$	$R^2 = 0.9994$	2.020	$m_{AT/tab.} = 5m' = 10.24$
Ibn Ai Haytham, Pharma Industries Co. Aleppo-SYRIA	20	$y = 12.61x + 25.649$	$R^2 = 0.9996$	2.034	$m_{AT/tab.} = 10m' = 20.34$
	40	$y = 12.62x + 25.593$	$R^2 = 0.9998$	2.028	$m_{AT/tab.} = 20m' = 40.56$
<i>Atoraz</i> , Ctd. tab.	10	$y = 12.60x + 24.494$	$R^2 = 0.9995$	1.944	$m_{AT/tab.} = 5m' = 9.72$
Razi pharmaceutical industries Aleppo-SYRIA	20	$y = 12.61x + 24.488$	$R^2 = 0.9966$	1.942	$m_{AT/tab.} = 10m' = 19.42$
	40	$y = 12.61x + 25.119$	$R^2 = 0.9999$	1.992	$m_{AT/tab.} = 20m' = 39.84$

*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 polarography at SMDE with negative amplitude in borax buffer at pH 7.5

Commercial name	Contents, mg/tab.	* \bar{X} , mg/tab.	Standard deviation SD, mg/tab.	RSD%	Analytical standard error $\frac{SD}{\sqrt{n}}$, mg/tab.	Confidence limit $x \pm \frac{t.SD}{\sqrt{n}}$, mg/tab.	Recovery %
Atorvex , Ctd. tab.	10	10.05	0.34	3.4	0.15	10.05±0.42	100.5
Asia pharmaceutical industries	20	20.60	0.68	3.3	0.30	20.60±0.83	103.0
Aleppo-SYRIA	40	42.00	1.34	3.2	0.59	42.00±1.66	105.0
Atorvatin , Ctd. tab.	10	9.70	0.34	3.5	0.15	9.70±0.41	97.0
Alpha Aleppo	20	19.80	0.65	3.3	0.29	19.80±0.82	99.0
Pharmaceutical Industries Aleppo-SYRIA	40	39.60	1.27	3.2	0.56	39.60±1.57	99.0
Lipito-med , Ctd. tab.	10	9.94	0.34	3.4	0.15	9.94±0.42	99.2
Medico Labs.	20	20.23	0.69	3.4	0.30	42.00±0.85	101.2
Homs-SYRIA	40	40.19	1.33	3.3	0.59	40.19±1.65	100.5
Liostatin , Ctd. tab.	10	10.24	0.36	3.5	0.16	10.24±0.44	102.4
Ibn Al Haytham , Pharma Industries Co.	20	20.34	0.69	3.4	0.30	20.34±0.85	101.7
Aleppo-SYRIA	40	40.56	1.30	3.2	0.58	40.56±1.61	101.4
Atoraz , Ctd. tab.	10	9.72	0.34	3.5	0.15	9.72±0.42	97.2
Razip pharmaceutical industries	20	19.42	0.66	3.4	0.29	19.42±0.81	97.1
Aleppo-SYRIA	40	39.84	1.35	3.4	0.60	39.84±1.66	99.6

*n=5

CONCLUSION

The differential pulse polarography (DPP) of atorvastatin (AT) in pure and pharmaceutical dosage forms in borax buffer media has been investigated using static mercury drop electrode (SMDE). One reduction peak was observed in the range -1340 to -1385 mV (E_p). The peak current I_p is linear over the ranges 0.2234-24.580 $\mu\text{g.mL}^{-1}$; the sensitivity increased to about 5 times higher than using dropping mercury electrode (DME). The relative standard deviation (RSD) did not exceed 3.2% for the concentrations of AT 0.2234 $\mu\text{g.mL}^{-1}$. Regression analysis showed a good correlation coefficient ($R^2=0.9999$) between I_p and concentration over the studied range with detection limit (LOD) and quantification limit (LOQ) of 0.024 and 0.071 $\mu\text{g.mL}^{-1}$, respectively. The proposed method was successfully applied to the analysis of AT in pure and pharmaceutical dosage forms with average recovery of 97.0 to 105.0%. The results obtained agree well with the contents stated on the labels.

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