Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 7, Issue 3, 2015

Original Article

THE EFFECT OF HANDING MERCURY DROP ELECTRODE ON DIFFERENTIAL PULSE POLAROGRAPHIC BEHAVIOR AND DETERMINATION OF ROSUVASTATIN IN PURE AND PHARMACEUTICAL TABLETS

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Received: 19 Dec 2014 Revised and Accepted: 10 Jan 2015

ABSTRACT

Objective: Developing a simple, accurate and very sensitive differential pulse polarographic method (DPPM) for determination of rosuvastatin (RSV) in pure and tablets dosage forms using handing mercury drop electrode (HMDE).

Methods: The DPPM was applied in Na_2HPO_4 buffer at pH 1.5 using a HMDE in optimal conditions.

Results: One redaction peak was observed in the range -929 to -940 mV (E_p). The peak current I_p is linear over the ranges 0.9631-192.61 ng. mL^{-1}; Which led to increase the sensitivity about ten and hundred times when using SMDE and DME, respectively. The relative standard deviation did not exceed 3.6% and regression analysis showed a good correlation coefficient (R^2= 0.9998). The limit of detection (LOD) and the limit of quantification (LOQ) were to be 0.112 and 0.34 ng. mL^{-1}, respectively. The amounts of RSV in different tablet dosage forms were decreases with the time (1.1-1.7% after six months at the end of the validity period).

Conclusion: The proposed method was successfully applied to determine very small amounts of RSV (0.9631 ng. mL^{-1}) in pure form and in pharmaceutical tablets.

Keywords: Differential pulse polarographic method, Handing mercury drop electrode, Rosuvastatin, Pharmaceutical tablets.

INTRODUCTION

Rosuvastatin calcium $(C_{22}H_{27}FN_3O_6S)_2Ca$, is a synthetic lipid lowering agent that is widely used to treat hypercholesterolemia and hyperlipidemia, mol. mass 1001.14 g, while rosuvastatin (RSV) is $C_{22}H_{28}FN_3O_6S$ and its mol. mass 481.539 g. Rosuvastatin calcium is a white amorphous powder [1-4]. Literature survey revealed that HPLC[5-7], capillary zone electrophoresis [8], spectrophotometry [9-12] and electrochemical methods [13-15] are available for rosuvastatin analysis in pure form and pharmaceutical preparations. The polarographic and voltammetric analysis was successfully applied for determination some drugs as atorvastatin [16-18], gatifloxacin[19], carbinoxamine maleate [20], dipyrone [21]and lomefloxacin [22].

The electrochemical behavior of rosuvastatin calcium was investigated using cyclic voltammetry (CV) and chronoamperometry (CA) methods. Rosuvastatin calcium's reduction peak was seen at −1184 mV in pH 5 acetate buffer with a hanging mercury drop electrode (HMDE). Linearity for rosuvastatin calcium was found between 0.20 and 10.00 μg mL^{-1}. While the LOD for rosuvastatin calcium was 0.07 μg mL^{-1}, the LOQ was 0.20 μg mL^{-1}. This method was applied (the first time) to the determination of RSV calcium from pharmaceutical preparations [13].

Electrochemical behavior and differential pulse polarographic analysis (DPPA) of rosuvastatin (RSV) in pure form and in pharmaceutical preparations using dropping mercury electrode (DME) with di-sodium hydrogen orthophosphate buffer was applied. One redaction peak was observed in the range -1081 to -1094 mV (E_p). The peak current I_p is linear over the ranges 0.0963-24.077 μg. mL^{-1}. The DPPA has been used successfully for the determination of RSV in pure form and in pharmaceutical formulations. The relative standard deviation did not exceed 4.0% for the concentrations of RSV 0.0963 μg. mL^{-1}. The limit of detection (LOD) and the limit of quantification (LOQ) were to be 0.0125 and 0.038 μg. mL^{-1}, respectively [14].

Differential pulse polarographic behavior and determination of rosuvastatin (RSV) in pure form and in pharmaceutical preparations at pH 1.5 with di-Sodium hydrogen orthophosphate buffer using a static mercury drop electrode (SMDE) was applied. One redaction peak was observed in the range -951 to -970 mV (E_p). The peak current I_p is linear over the ranges 9.631-1926.10 ng. mL^{-1}. The relative standard deviation did not exceed 3.8%. Regression analysis showed a good correlation coefficient (R^2= 0.9999). The LOD and the LOQ were to be 1.22 and 3.70 ng. mL^{-1}, respectively. The proposed method was successfully applied to the analysis of RSV in pure and pharmaceutical dosage forms with average recovery of 92.50 to 101.35%. The amount of RSV in different pharmaceutical preparations were decreases with the time (2-3% after one year) and the relative decrease was more in the tablets which contain lesser amounts of RSV[15].

In the present work, the effect of handing mercury drop electrode (HMDE) on differential pulse polarographic behavior and determination of rosuvastatin in pure and pharmaceutical tablets forms was applied.

MATERIALS AND METHODS

Reagents

di-Sodium hydrogen orthophosphate and phosphoric acids, were purchased from Merck. Rosuvastatin calcium (98.6%) was supplied by BDR Pharmaceuticals International PVT. LTD. (India), its purity as rosuvastatin was 94.66%. Ultrapure mercury from Metrohm Company was used throughout the experiments.

Supporting electrolyte

Di-Sodium hydrogen orthophosphate of 0.075 mol. L^{-1} and H_3PO_4 was prepared by adding H_3PO_4 (1.0 M) to pH=1.5.

A stock standard solution of Rosuvastatin calcium ($1x10^{-6}$ mol. L^{-1})

This solution was prepared by dissolving 25.38 mg from rosuvastatin calcium in 50 mL double distilled deionized water ($1x10^{-3}$ mol. L^{-1}) then dilute 0.100 mL from this solution to 100 mL ($1x10^{-6}$ mol. L^{-1} or 0.481539 μg. mL^{-1}).

Working solutions

The stock solution was further diluted to obtain working solutions daily just before use in the ranges of RSV: 2.0, 4.0, 6.0, 10.0, 20.0,

40.0, 80.0, 100.0, 150.0, 200.0, 250.0, 300.0, 350.0 and 400.0 nmol.L^{-1} (0.9631, 1.926, 2.889, 4.815, 9.631, 19.26, 38.52, 48.15, 72.23, 96.31, 120.38, 144.46,168.54 and 192.61 ng. mL^{-1}) by dilution of the volumes: 0.050, 0.100, 0.150, 0.250, 0.500, 1.000, 2.000, 2.500, 3.750, 5.000, 6.250, 7.500, 8.750 and 10.000 mL from stock standard solutions to 25 mL with supporting electrolyte. All solutions and reagents were prepared with double-distilled de ionised water and analytical grade chemicals.

Instruments and apparatus

A Metrohm 746 VA processor, A Metrohm 747 VA stand with a Handing mercury drop electrode (HMDE) as a working electrode, 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 ^{o}C. Highly pure nitrogen gas (99.999 %) was used for de-oxygenation. pH meter from Radiometer 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 PIPTMAN P, GILSON), were used for preparation of the experimental solutions. A ultrasonic processor model power sonic 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) was used for the analysis of rosuvastatin (RSV) by using DPPM with HMDE. The pharmaceutical formulations were subjected to the analytical procedures:

(1) *Rosuvastatin-ElSaad* tablets, ELSaad pharma, Aleppo–SYRIA, each tablet contains: 10, 20 and 40 mg of RSV (Mfg. 04/2012 and Exp. 04/2016).

(2) *Rosuva* tablets, Unipharma, Damascus–SYRIA, Each tablet contains: 5, 10 and 20 mg of RSV (Mfg. 11/2011 and Exp. 11/2015).

(3) *Rosuvastatin Sandy* tablets, Sandy pharmaceuticals, Aleppo – SYRIA, Each tablet contains: 10, 20 and 40 mg of RSV (Mfg. 07/2012 and Exp. 07/2016).

(4) *Turbovas* tablets, City Pharma Co., Aleppo–SYRIA, each tablet contains: 10 and 20 mg of RSV (Mfg. 03/2012 and Exp. 03/2016).

(5) Crostatin tablets, Razi pharmaceutical industries, Aleppo–SYRIA, each tablet contains: 5, 10 and 20 mg of RSV (Mfg. 11/2011 and Exp. 11/2015).

Stock solutions of pharmaceutical formulations

Ten tablets of each studied pharmaceutical formulations were accurately weighed and powdered. The amount equivalent to tenth the weight of one tablet was weighed and solved in 100 ml double-distilled de ionised water by using ultrasonic bath for 15 min at 25^{o}C, filtered over a 500 mL flask and diluting to 500 mL with water, which content as the follows: 1, 2, 4 and 8 µg. mL^{-1} for all studied pharmaceutical formulations content 5, 10, 20 and 40 mg/tab, respectively. Appropriate solutions were prepared by taking suitable aliquots into supporting electrolyte.

Working solutions of pharmaceuticals

These solutions were prepared daily by diluting 1.000, 0.500, 0.250 and 0.125 mL from stock solutions of pharmaceutical formulations, respectively, then diluting to 50 mL with supporting electrolyte; each solution contents 0.020 µg. mL^{-1} (20 ng. mL^{-1}) of rosuvastatin.

Working standard addition solutions of pharmaceuticals

Standard addition solutions of pharmaceuticals tablets were prepared as the follows: same mentioned volumes of stock solutions of pharmaceuticals with 0.000, 2.000, 4.000, 6.000 and 8.000 mL from stock solution of rosuvastatin and diluting to 50 mL with supporting electrolytes; these solutions content (each one) 20 ng. mL^{-1} of RSV (from pharmaceuticals) plus 19.261, 38.52, 57.785 and 77.046 ng. mL^{-1} of RSV (from standard solutions), respectively.

Analytical procedure

25 mL of working standard solution of rosuvastatin was transferred to the cell. The solution was well mixed by automatic mixer and de oxygenated with N_2 gas for 100 s. Current-voltage curves were recorded and all the measurements were depended from the second polarogram. Limiting currents in supporting electrolytes were measured. Calibration and standard addition curves of RSV in pure form and in pharmaceutical tablets were constructed.

RESULTS AND DISCUSSION

Differential pulse polarographic behavior

The polarograms in the optimal conditions (supporting electrolytes, pH, scan rate, initial potential, final potential etc.) using DPPM at HMDE were studied. The reduction mechanism of RSV was investigated. The reduction step is expressed with a heterocyclic ring. It is proposed that the transfer of two electrons related to the reduction of RSV observed at -929 to -940 mV occurred on the nitrogen–carbon double bond of the pyrimidine ring [15].

The effect of supporting electrolytes and pH

The type of supporting electrolyte and pH of the media are very important for differential pulse polarographic method. Various buffers were examined as supporting electrolytes for differential pulse polarographic behavior of RSV. The results showed that the di-sodium hydrogen orthophosphate (Na_2HPO_4) Buffer at pH 1.5 gave the optimum signal response (the better buffer at concentration 0.075 mol. L^{-1}). Peak current (I_p) and potential peak (E_p) significantly effect with the values of pH solution (from 0.4 to 2.0). The values of I_p increase with increasing pH value of 0.40 to 1.25 then become semi-fixed until pH 1.75 after that decrease to pH=2.00, see fig. (1). E_p values are growing a negative value from -885 mV (when pH = 0.40) to -968 mV (when pH = 2.00).

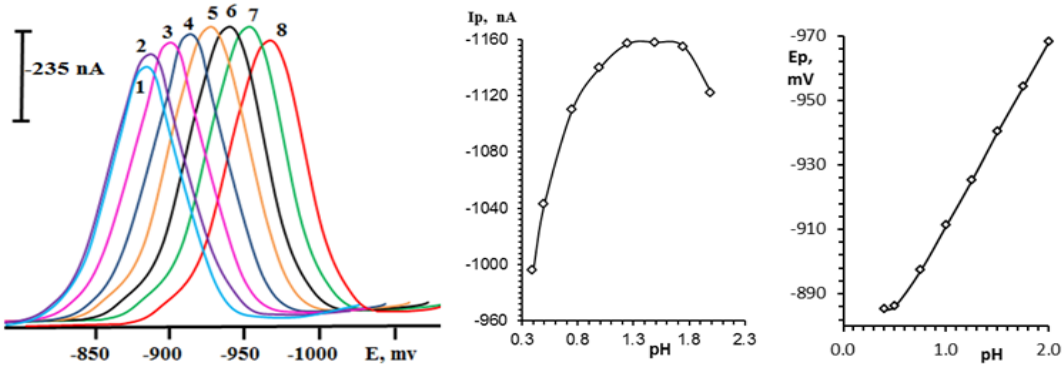

Fig. 1: The effect of pH solution at: 0.40; 0.50; 0.75; 1.00; 1.25; 1.50; 1.75 and 2.00 (curves 1-8) on the polarograms (a), I_p (b) and E_p (c) of RSV (192.61 ng. mL^{-1}) using DPPM at HMDE (Purge gas N_2, Purge time 100 s, Scan rate 6.667 mV/s, U. amplitude -90 mV, U. step 10 mV, t. meas 32 ms, t. pulse 35 ms, t. step 1.5 s, U. meas -300 mV, temperature 25°± 5°C and Na_2HPO_4 buffer)

The effect of negative pulse amplitude (U. ampl)

The effect of negative pulse amplitude between -10 to -100 mV on I_p showed that, I_p slowly increases with increasing amplitude until -40 mV then becomes a linear increase until -90 mV after that deviate from the linear, while E_p values are growing a negative value from -927 mV (when U. ampl = -10 mV) to -944 mV (when U. ampl = -60 mV), then become semi-fixed until U. ampl = -70 mV and after that decrease to -939 mV (when U. ampl = -100 mV), fig. (2).

The effect of time pulse (t. pulse)

The effect of time pulse (35, 40, 45, 50, 60, 70, 80, 90, 100 ms) on polarograms of RSV was as the follows: with increasing t. pulse the values of I_p decreases and E_p has become increasingly to positive values (from -940 to -920 mV). When the t. pulse value of 35 ms I_p was more symmetrical and its value was max, see fig. (3).

The effect of time interval for voltage step (t. step)

The effect of t. step (0.2, 0.3, 0.4, 0.5, 0.6, 0.8, 1.0, 1.5, 2.5 and 3.5 s) on I_p and E_p was studied. I_p increases (from -319 nA when t. step = 0.2 s) with increasing t. step to 2.5 s (I_p=-942 nA), after that decrease to -711 nA (when t. step = 3.5 s), fig. (4, b), while E_p remains quasi-static from t. step 0.2 to1.5 s, after that increase to -960 mV (when t. step = 3.5 s), The value of the preferred t. step was 1.5 s, see fig. (4, c).

The effect of measurement time (t. meas)

The effect of measurement time (t. meas) at values (4, 6, 10, 14, 20, 24, 28, 30 and 32 ms) on the polarograms of RSV using DPPM at HMDE was studied. I_p slowly increases with increasing t. meas, while E_p remains quasi static (E_p=-936 mV) from t. meas equals 4 to 20 ms, after that increasingly negative even at -940 mV (when t. meas = 32 ms). The value of the preferred t. meas was 32 ms.

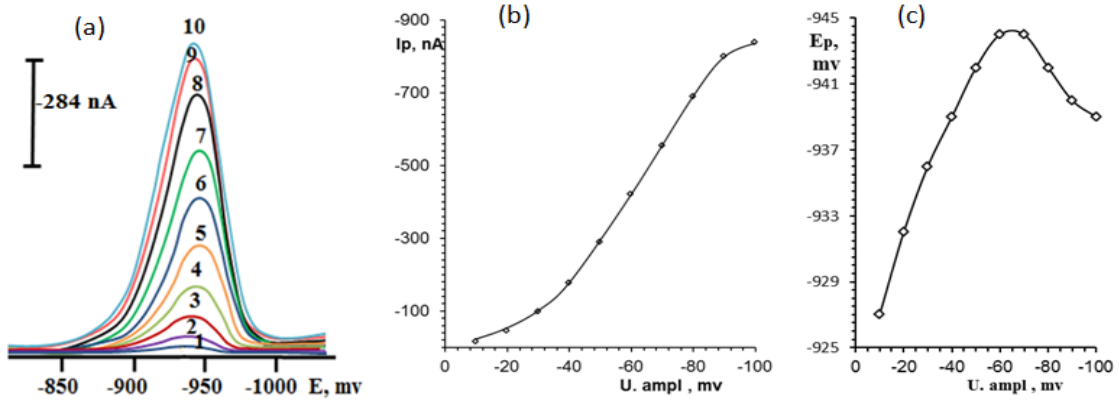

Fig. 2: The effect of negative pulse amplitude (U. ampl) at: - 10; -20; -30; -40; -50; -60; -70; -80; -90 and -100 mV (curves 1-10) on the polarograms (a), I_p (b) and E_p (c) of RSV (192.61 ng. mL^{-1}) using DPPM at HMDE (Purge gas N_2, Purge time 100 s, Scan rate 6.667 mV/s, U. step 10 mV, pH=1.5, t. meas 32 ms, t. pulse 35 ms, t. step 1.5 s, U. meas -300 mV, temperature 25°± 5°C and Na_2HPO_4 buffer)

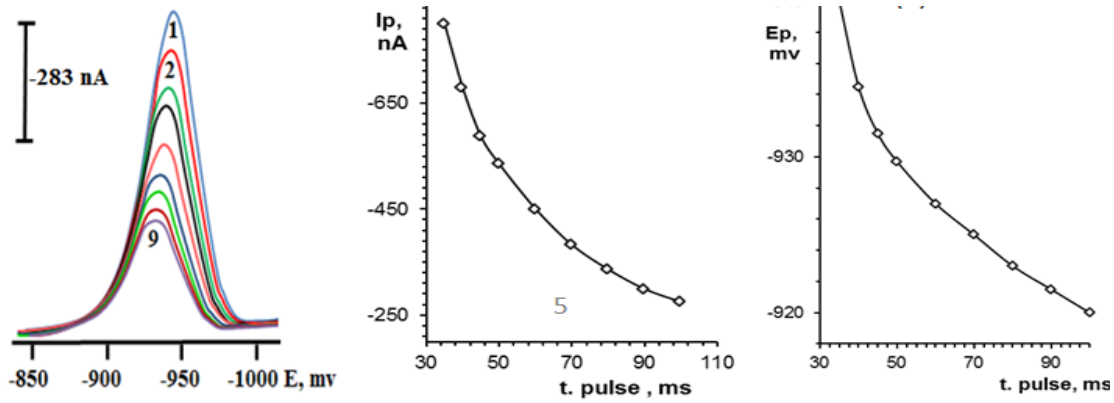

Fig. 3: The effect of time pulse (t. pulse) at: 35, 40, 45, 50, 60, 70, 80, 90 and 100 ms (curves 1-9) on the polarograms (a), I_p (b) and E_p (c) of RSV (192.61 ng. mL^{-1}) using DPPM at HMDE (Purge gas N_2, Purge time 100 s, Scan rate 6.667 mV/s, U. step 10 mV, pH=1.5, t. meas 32 ms, U. amplitude -90 mV, t. step 1.5 s, U. meas -300 mV, temperature 25°± 5°C and Na_2HPO_4 buffer)

The effect of voltage step (U. step) and sweep rate

The different values of voltage step (U. step) at values (2, 4, 6, 8, 10 and 12 mV) and sweep rate at 1.33 to 8.00 mV/s were studied. I_p remains increases linearly from 2 to 10 then deviates from the linear. E_p increases in a non-linear by negative value (E_p=-917 mV to -941 mV) from U. step equals 2 to 12 mV. It was found that, the value of U. step 10 mV and sweep rate 6.667 mV/s were the best, see fig. (5).

The effect of measurement voltage (U. meas)

I_p increases from -232 to -800 nA and E_p also increases of a negative value from -935 to -940 mV by changing U. meas from 0 to -200 mV, then I_p and E_p remain constant until U. meas=-600 mV. It was found that, the value of U. meas -300 mV was the best, see fig. (6).

The effect of drop size

I_p increases with increasing drop size from 1 to 9, while E_p has become proximal constant (-938 to -940 mV) with increasing drop size. The value of the preferred drop size was 9.

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 -800 mV and better final potential was -1100 mV.

The effect of temperature and time

The effect of temperature and time on the electrochemical reaction of rosuvastatin 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°C (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.

The optimum parameters established for determination of RSV using DPPM on HMDE, SMDE [15] and DME [14] showed in table 1

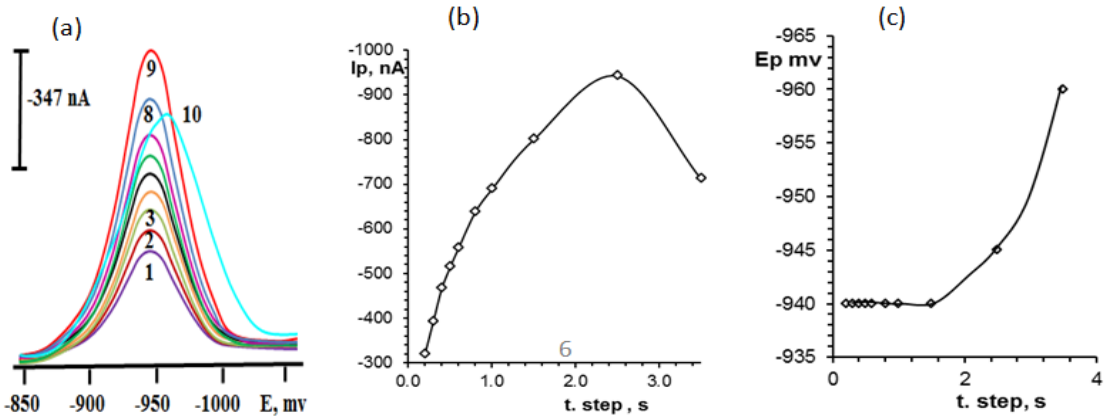

Fig. 4: The effect of time interval for voltage step (t. step) at: 0.2, 0.3, 0.4, 0.5, 0.6, 0.8, 1.0, 1.5, 2.5 and 3.5 s (curves 1-10) on the polarograms (a), I_p (b) and E_p (c) of RSV (192.61 ng. mL^{-1}) using DPPM at HMDE (Purge gas N_2, Purge time 100 s, pH=1.5, t. meas 32 ms, U. amplitude -90 mV, t. pulse 35 ms, U. meas -300 mV, temperature 25°± 5°C and Na_2HPO_4 buffer)

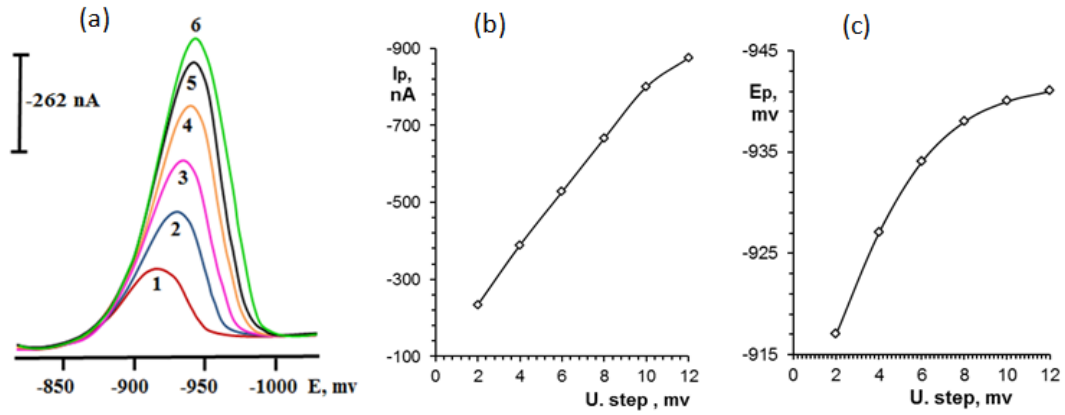

Fig. 5: The effect of voltage step (U. step) 2, 4, 6, 8, 10 and 12 mV and sweep rate (curves 1-6) on the polarograms (a), I_p (b) and E_p (c) of RSV (192.61 ng. mL^{-1}) using DPPM at HMDE (Purge gas N_2, Purge time 100 s, pH=1.5, t. meas 32 ms, U. amplitude -90 mV, t. pulse 35 ms, U. meas -300 mV, temperature 25°± 5°C and Na_2HPO_4 buffer)

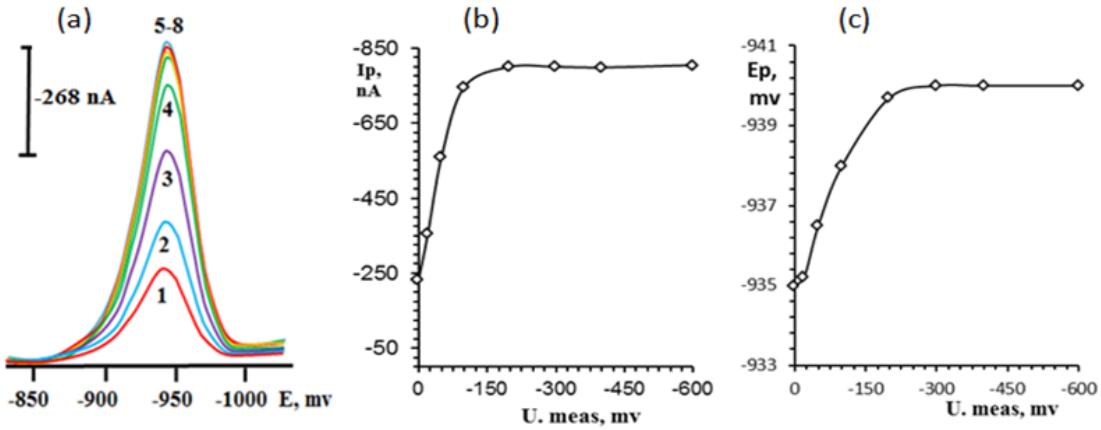

Fig. 6: The effect of U. meas 0, -20, -50, -100, -200, -300, -400 and -600 mV (curves 1-8) on the polarograms (a), I_p (b) and E_p (c) of RSV (192.61 ng. mL^{-1}) using DPPM at HMDE (Purge gas N_2, Purge time 100 s, Scan rate 6.667 mV/s, pH=1.5, t. meas 32 ms, U. amplitude -90 mV, t. pulse 35 ms, U. step 10 mV, t. step 1.5 s, temperature 25°± 5°C and Na_2HPO_4 buffer)

Table 1: The optimum parameters established for determination of RSV using DPPM on HMDE, SMDE [15] and DME [14] in optimum conditions

Parameters	Operating modes		
	HMDE	SMDE [15]	DME [14]
Supporting electrolytes (buffer)	Di-sodium hydrogen orthophosphate Na_2HPO_4 (0.075 mol. L^{-1})		
Solvent rosuvastatin calcium	double distilled deionized water		
pH	1.5		
Purge gas	Pure N_2		
Initial potential	-800 mV		
Final potential	-1200 mV		
Temperature of solution	25°± 5°C		
Value of pulse amplitude	-90 mV	-90 mV	-60 mV
Purge time	100 s	100 s	200 s
U. step	10 mV	8 mV	6 mV
Scan (sweep) rate	6.667 mV/s	5.0 mV/s	6.667 mV/s
t. meas	32 ms	32 ms	20 ms
t. pulse	35 ms	40 ms	60 ms
t. step	1.5 s	1.6 s	0.9 s
U. meas	-300	-	-
Peak Potential, mV	-929 to -940 mV	-951 to -970 mV	-1081 to -1094 mV
LOD(3.3SD)	0.112 ng. mL^{-1}	1.22 ng. mL^{-1}	12.5 ng. mL^{-1}
LOQ (10SD)	0.34 ng. mL^{-1}	3.70 ng. mL^{-1}	38.0 ng. mL^{-1}
Linearity range of concentration	0.9631 to 192.61 ng. mL^{-1}	9.631 to 1926.10 ng. mL^{-1}	0.0963 to 24.077 µg. mL^{-1}
Regression equation:	*y=-4.1565x*-3.7043	*y=-0.5737x*-0.8577	*y=-125.06x**-10.02
Slope	-4.1565	-0.5737	-125.06
Intercept	-3.7043	-0.8577	-10.02
Correlation coefficient (R^2)	0.9998	0.9999	0.9998
RSD	3.6%	3.8%	4.0%

* y= nA, **x***= concentration of RSV by ng. mL^{-1} and **x****= concentration of RSV by µg.mL^{-1}.

Calibration curves

Calibration curves for the determination of rosuvastatin using differential pulse polarographic method on HMDE with negative amplitude at pH1.5 with di-sodium hydrogen orthophosphate buffer were applied. One redaction peak was observed in the range -929 to -940 mV (Ep). The peak current (I_p) was proportional to the concentration of RSV over the ranges 0.9631-192.61 ng. mL^{-1} (0.0020–0.400 µmol. L^{-1}). The polarograms in the optimum conditions using DPPM at HMDE of RSV at different concentrations show in fig. 7. The regression equation and correlation coefficient (R^2) were as the follows: y=-4.1565x-3.7043, R^2=0.9998; where y: I_p, nA and x: C_{RSV}, ng. mL^{-1}, see fig. 8.

Analytical results

Determination of RSV using DPPM on HMDE under the optimum conditions using analytical curves, $I_p=f(C_{RSV})$, showed that the accuracy was ready over the ranges of RSV concentration between 0.9631–192.61 ng. mL^{-1}. The relative standard deviation (RSD) not more than 3.6%, see table 2. Limit of detection (LOD) and limit of quantitation (LOQ) for the determination of RSV by this method were as the follows: 0.112 and 0.34 ng. mL^{-1}, respectively.

Table 2 shows that, the results of the concentrations of RSV which are largest of 192.61 ng. mL^{-1} become non-linear and non-acceptable (the average concentration of RSV is less than the standard concentration; when the concentration of RSV 240.75 ng. $mL^{-1}$is less about 4% and at the concentration 288.91 ng. mL^{-1} is less about 7%).

Repeatability

The repeatability of the method was evaluated by performing 10 repeat measurements for 96.308 ng. mL^{-1} of RSV using DPPM on HMDE under the optimum conditions. The amount of RSV was found to be 95.074 ± 1.88 and the percentage recovery was found to be 98.72 ± 1.9 with RSD of 0.020. These values indicate that the proposed method has high repeatability and precision for RSV analysis.

Application

Many applications for the determination of rosuvastatin in some Syrian pharmaceutical preparations using differential pulse polarographic method on handing mercury drop electrode with negative amplitude in di-sodium hydrogen orthophosphate buffer at pH=1.5 were proposed.

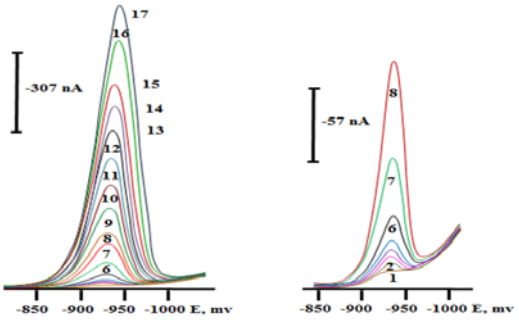

Fig. 7: The polarograms in the optimum conditions using DPPM on HMDE of RSV in Na_2HPO_4 buffer (pH 1.5) at concentrations: 1- 0; 2- 0.9631; 3- 1.926; 4- 2.889; 5- 4.82; 6- 9.63; 7- 19.26; 8- 38.52; 9- 48.15; 10- 72.23; 11- 96.31; 12- 120.38; 13- 144.46; 14- 168.54; 15- 192.61; 16- 240.75 and 17- 288.91 ng. mL^{-1}

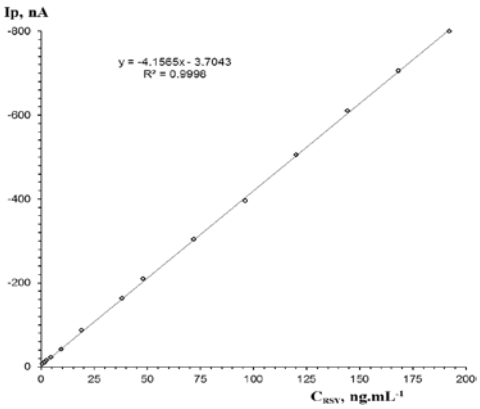

Fig. 8: Calibration curves for the determination of RSV using DPPM on HMDE under the optimum conditions.

Table 2: Determination of rosuvastatin using DPPM on HMDE with negative amplitude in Na_2HPO_4 buffer (0.075 mol. L^{-1})at pH 1.5

x_i, ng. mL^{-1} (Taken)	$\overline{X}$ *, ng. mL^{-1} (Found)	SD, ng. mL^{-1}	$\frac{SD}{\sqrt{n}}$, ng. mL^{-1}	$\overline{x} \pm \frac{t.SD}{\sqrt{n}}$, ng. mL^{-1}	RSD %
0.9631	0.958	0.034	0.015	0.958± 0.043	3.6
1.926	1.82	0.062	0.028	1.819± 0.077	3.4
2.89	2.80	0.089	0.040	2.802± 0.111	3.2
4.82	4.78	0.14	0.063	4.782± 0.174	3.0
9.63	9.24	0.26	0.12	9.240± 0.32	2.8
19.26	20.01	0.50	0.22	20.013± 0.62	2.5
38.52	38.52	0.92	0.41	38.520± 1.15	2.4
48.15	49.46	1.09	0.49	49.457± 1.35	2.2
72.23	73.87	1.55	0.69	73.87± 1.92	2.1
96.31	94.98	1.90	0.85	94.984± 2.36	2.0
120.38	120.79	2.17	0.97	120.79± 2.69	1.8
144.46	146.81	2.50	1.12	146.806± 3.10	1.7
168.54	169.76	2.88	1.29	169.76± 3.57	1.7
192.61	190.70	3.43	1.53	190.696± 4.26	1.8
240.75	231.39	8.10	3.62	231.39± 10.05	3.5
288.91	268.50	15.57	6.96	268.50± 19.33	5.8

* n=5, t=2.776.

Standard addition curves for determination of RSV in different Syrian pharmaceutical preparations (*Rosuvastatin-ElSaad*, *Rosuva*, *Rosuvastatin Sandy*, *Turbovas* and *Crostatin*) were used. The standard addition curve of *Rosuvastatin-ElSaad* (20 mg/tab.) was showed in fig. 9, as an example. Regression equations and correlation coefficients were included in table 3.

Standard addition curves for determination of RSV in different Syrian pharmaceutical tablets were used. The amount (m) of RSV in one tablet by mg/tab (m_{RSV}/tab.) calculated from the following relationship: m = h. m', where: m' is the amount of RSV in tablet, which calculated from the standard additions curve according to the following regression equation: y=a. x+b; when y=0; m'=x= b/a= intercept/slope (ng. mL^{-1}) and h conversion factor is equal to 0.25, 0.5, 1.0 and 2.0 for all mentioned pharmaceutical preparations which content 5, 10, 20 and 40 mg/tab, respectively. The results of quantitative analysis for RSV in the pharmaceutical tablets using this method were included in Tables 4.

It was found that, the amount of RSV in different pharmaceutical preparations were decreases with the time (1.1-1.7% after one six months; June 2014[15] to December 2014, store at room temperature 20-30°C) and the relative decrease was more in the tablets which contain lesser amount of RSV, see fig. 10 and tables 5.

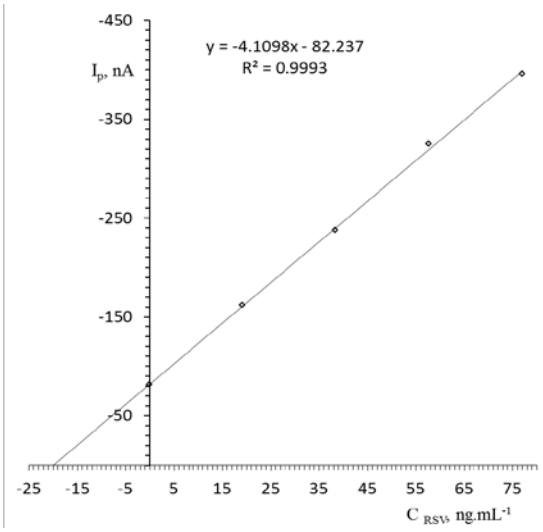

Fig. 9: standard addition curve of *Rosuvastatin-ElSaad* (20 mg/tab)

Table 3: Regression equations and correlation coefficients for determination of rosuvastatin in Syrian pharmaceutical tablets using DPPM on HMDE with negative amplitude in Na_2HPO_4 buffer at pH 1.5

Pharmaceutical preparations	RSV In tab., mg	Operating modes			
		Regression equations*	Correlation coefficients	m', ng. mL^{-1}	Amount of rosuvastatin (m), mg/tab.
Rosuvastatin-ElSaad tablets, ELSaad pharma, Aleppo–SYRIA	10	y=-4.1602x-79.451	R^2=0.9992	19.098	$m_{RSV/tab.}$=0.5m'=9.549
	20	y=-4.1098x-82.237	R^2=0.9993	20.020	$m_{RSV/tab.}$=1.0m'=20.02
	40	y=-4.1227x-79.238	R^2=0.9994	19.220	$m_{RSV/tab.}$=2.0m'=38.44
Rosuva tablets, Unipharma, Damascus–SYRIA	5	y=-4.1706x-75.827	R^2=0.9990	18.184	$m_{RSV/tab.}$=0. 25m'=4.546
	10	y=-4.1289x-78.920	R^2=0.9993	19.114	$m_{RSV/tab.}$=0. 5m'=9.557
	20	y=-4.1753x-82.128	R^2=0.9994	19.670	$m_{RSV/tab.}$=1.0m'=19.67
Rosuvastatin Sandy tablets, Sandy pharmaceuticals, Aleppo –SYRIA	10	y=-4.1086x-79.36	R^2=0.9992	19.316	$m_{RSV/tab.}$=0. 5m'=9.658
	20	y=-4.1185x-76.110	R^2=0.9993	18.480	$m_{RSV/tab.}$=1.0m'=18.48
	40	y=-4.1521x-79.950	R^2=0.9995	19.255	$m_{RSV/tab.}$=2.0m'=38.51

Turbovas tablets, City Pharma Co., Aleppo–SYRIA	10	y=-4.1600x-80.504	R^2=0.9992	19.352	$m_{RSV/tab.}$=0. 5m'=9.676
	20	y=-4.1487x-82.51	R^2=0.9994	19.890	$m_{RSV/tab.}$=1.0m'=19.89
Crostatin tablets, Razi pharmaceutical industries, Aleppo–SYRIA	5	y=-4.1621x-75.70	R^2=0.9990	18.188	$m_{RSV/tab.}$=0. 25m'=4.547
	10	y=-4.1554x-81.97	R^2=0.9992	19.726	$m_{RSV/tab.}$=0. 5m'=9.863
	20	y=-4.1824x-79.93	R^2=0.9994	19.110	$m_{RSV/tab.}$=1.0m'=19.11

*y= nA, x= concentration of RSV (ng. mL^{-1})= m' = intercept/slope.

Table 4: Determination of rosuvastatin in Syrian pharmaceutical tablets using DPPM on HMDE with negative amplitude in Na_2HPO_4 buffer at pH 1.5

Commercial name	Contents, mg/tab.	* $\bar{x}$, mg/tab.	RSD%	Recovery %
Rosuvastatin-ElSaad tablets, ELSaad pharma, Aleppo–SYRIA	10	9.549	3.0	95.49
	20	20.02	2.9	100.10
	40	38.44	2.7	96.10
Rosuva tablets, Unipharma, Damascus–SYRIA	5	4.546	3.2	90.92
	10	9.557	2.9	95.57
	20	19.67	2.8	98.35
Rosuvastatin Sandy tablets, Sandy pharmaceuticals, Aleppo –SYRIA	10	9.658	3.0	96.58
	20	18.48	2.8	92.40
	40	38.51	2.7	96.27
Turbovas tablets, City Pharma Co., Aleppo–SYRIA	10	9.676	2.9	96.76
	20	19.89	2.8	99.45
Crostatin tablets, Razi pharmaceutical industries, Aleppo–SYRIA	5	4.547	3.3	90.94
	10	9.863	3.0	98.63
	20	19.11	2.8	95.55

* n=5

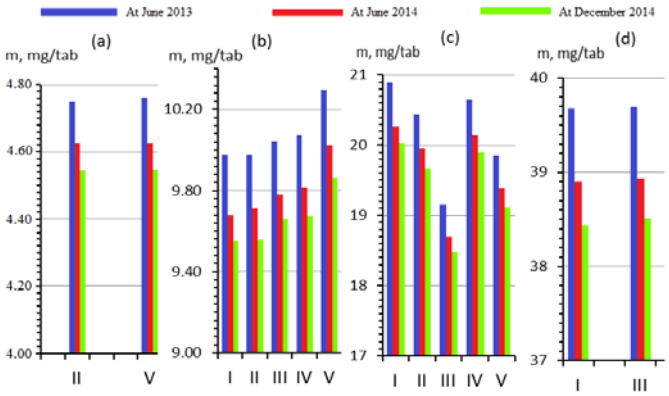

Fig. 10: The effect of time on rosuvastatin content in Syrian pharmaceutical tablets content: (a) 5, (b) 10, (c) 20 and (d) 40 mg/tab (I- Rosuvastatin-ElSaad, II- Rosuva, III- Rosuvastatin Sandy, IV- Turbovas and V- Crostatin)

Table 5: The effect of time on rosuvastatin content in Syrian pharmaceutical tablets

Commercial name	Mfg.	Exp.	Meas. time	*Assay% Label claim content, mg/tab.			
				5	10	20	40
Rosuvastatin-ElSaad tablets	04/2012	04/2016	June 2013 [14]	-	99.74	104.50	99.19
			June 2014 [15]	-	96.80	101.35	97.26
			December 2014	-	95.49	100.10	96.10
Rosuva tablets	11/2011	11/2015	June 2013 [14]	95.00	99.75	102.20	-
			June 2014 [15]	92.50	97.12	99.75	-
			December 2014	90.92	95.57	98.35	-
Rosuvastatin Sandy tablets	07/2012	07/2016	June 2013 [14]	-	100.42	95.80	99.24
			June 2014 [15]	-	97.80	93.50	97.34
			December 2014	-	96.58	92.40	96.27
Turbovas tablets	03/2012	03/2016	June 2013 [14]	-	100.73	103.23	-
			June 2014 [15]	-	98.13	100.75	-
			December 2014	-	96.76	99.45	-
Crostatin tablets	11/2011	11/2015	June 2013 [14]	95.22	102.97	99.24	-
			June 2014 [15]	92.52	100.23	96.90	-
			December 2014	90.94	98.63	95.55	-

*n=5, Assay= Found content/ Label claim content.

The statistical comparison of differential pulse polarographic method results using HMDE under the optimum conditions with spectrophotometric analysis results [11,12] were done. The results

were compared with spectrophotometric methods reported in the literature and no significant difference was found statistically.

The proposed method was simple, economic, accurate, very sensitive and successfully applied to the determination of rosuvastatin in pure form and in pharmaceutical preparations.

CONCLUSION

Differential pulse polarographic behavior and determination of RSV in pure form and in pharmaceutical tablets with Na_2HPO_4 buffer at pH 1.5 using a HMDE was applied. One redaction peak was observed in the range -929 to -940 mV (E_p). The peak current I_p is linear over the ranges 0.9631-192.61 ng. mL^{-1}; which led to increase the sensitivity about ten and hundred times when using SMDE and DME, respectively. The relative standard deviation did not exceed 3.6% and regression analysis showed a good correlation coefficient (R^2= 0.9998). The limit of detection (LOD) and the limit of quantification (LOQ) were to be 0.112 and 0.34 ng. mL^{-1}, respectively. The amounts of RSV in different tablet dosage form were decreases with the time (1.1-1.7% after six months at the end of the validity period). The results were compared with a spectrophotometric methods reported in the literature and no significant difference was found statistically.

CONFLICT OF INTERESTS

Declared None

REFERENCES

1. Mori Y, Kuriyama G, Tanaka T, Tajima N. Usefulness of aggressive lipid-lowering therapy with rosuvastatin in hypercholesterolemic patients. Endocrine 2009;36(3):412-8.
2. Nissen S, Nicholls S, Sipahi I, Libby P, Raichlen JS, Ballantyne CM. Effect of very high-intensity statin therapy on regression of coronary atherosclerosis. Asteroid Trial JAMA 2006;295(13):1556-65.
3. Lennernas H, Fager G. Pharmacodynamics and pharmacokinetics of the HMG-CoA reductase inhibitors. Clin Pharmacokinet 1997;32:403-25.
4. Jones PH, Davidson MH, Stein EA, Bays HE, McKenney JM, Miller E. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses. Am J Cardiol 2003;92(2):152-1604.
5. Mehta TN, Patel AK, Kulkarni GM, Suubbaiah G. Determination of rosuvastatin in the presence of its degradation products by a stability indicating LC method. JAOAC Int 2005;88(4):1142-47.
6. Beludari MI, Prakash KV, Mohan GK. RP-HPLC method for simultaneous estimation of rosuvastatin and ezetimibe from their combination tablet dosage form. Int J Chem Analyt Sci 2013;4(4):205-9.
7. Kaila HO, Ambasana MA, Thakkar RS, Saravaia HT, Shah AK. A new improved RP-HPLC method for assay of rosuvastatin calcium in tablets. Indian J Pharm Sci 2010;72(5):592–98.
8. Suslu I, Celebier M, Altnoz S. Determination of rosuvastatin in pharmaceutical formulations by capillary zone electrophoresis. Chromatographia 2007;66:65-72.
9. Uyar B, Celebier M, Altinoz S. Spectrophotometric determination of rosuvastatin calcium in tablets. Pharm 2007;62:411-13.
10. Afroz A, Haque T, Uddin Talukder MdM, Ashraful Islam SM. Spectrophotometric estimation of rosuvastatin calcium and glimepiride in tablet dosage form. Asian J Pharm Anal 2011;1(4):74-8.
11. Ergin G, Caglar S, Onal A, Erturk toker S, Spectrophotometric determination of 3-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitors in pharmaceutical preparations. Turkish J Chem 2013;37:171-81.
12. Ramadan AA, Mandil H, Alshelhawi N. Spectrophotometric determination of rosuvastatin calcium in pure form and pharmaceutical formulations by the oxidation using iodine and formation triiodide complex in acetonitrile. Int J Pharm Pharm Sci 2014;6(5):579-85.
13. Sacide A, Banu U. Electrochemical behaviour and voltammetric determination of rosuvastatin calcium in pharmaceutical preparations using a square-wave voltammetric method. Anal Methods 2013;5(20):5709-16.
14. Ramadan AA, Mandil H, Ghazal N. Electrochemical behavior and differential pulse polarographic determination of rosuvastatin in pure form and in pharmaceutical preparations using dropping mercury electrode. Int J Pharm Pharm Sci 2014;6(3):128-33.
15. Ramadan AA, Mandil H, Ghazal N. Differential pulse polarographic behavior and determination of rosuvastatin in pure form and in pharmaceutical preparations using a static mercury drop electrode. Int J Pharm Pharm Sci 2015;7(1):389-96.
16. Ramadan AA, Mandil H, Hafez B. Differential pulse polarography of atorvastatin in pure and pharmaceutical dosage forms using static mercury drop electrode. Int J Pharm Pharm Sci 2013;5(1):434-40.
17. Ramadan AA, Mandil H, Hafez B. Differential pulse polarographic determination of atorvastatin in pharmaceutical dosage forms using dropping mercury electrode. Asian J Chem 2013;25(6):3467-72.
18. Ramadan AA, Mandil H, Hafez B. Effect of hanging mercury drop electrode on differential pulse polarographic analysis of atorvastatin in pharmaceuticals using borax buffer at pH7.50. Int J Pharm Pharm Sci 2012;4(Suppl 5):540-6.
19. Ramadan AA, Mandil H. Determination of gatifloxacin in pure form and pharmaceutical formulations by differential pulse polarographic analysis. Anal Biochem 2010;404:1-7.
20. Ramadan AA, Mandil H, Genco T. Determination of carbinoxamine maleate in pharmaceuticals by direct and differential pulse polarography. Asian J Chem 2009;21(9):7387-97.
21. Ramadan AA, Mandil H, Hafez B. Determination of dipyrone in pure form and pharmaceutical formulations by differential pulse polarographic analysis. Asian J Chem 2011;21(1):403-06.
22. Ramadan AA, Mandil H. Determination of lomefloxacin in pharmaceuticals using differential pulse polarographic analysis. Int J Pharm Pharm Sci 2012;4(Suppl 5):255-61.