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Original Article

SPECTROPHOTOMETRIC DETERMINATION OF ROSUVASTATIN IN PURE FORM AND PHARMACEUTICAL FORMULATIONS THROUGH ION-PAIR COMPLEX FORMATION USING BROMOCRESOL GREEN

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ABSTRACT

Objective: A simple, direct and accurate spectrophotometric method has been developed for the determination of rosuvastatin (RSV) in pure and pharmaceutical formulations by complex formation with bromocresol green (BCG).

Methods: The method involves the formation of a yellow ion-pair complex between rosuvastatin (RSV) and bromocresol green (BCG) reagent in chloroform.

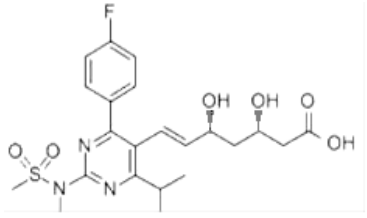
Results: The formed complex was measured at λ_{max} 416 nm against the reagent blank prepared in the same manner. Variables were studied in order to optimize the reaction conditions. Beer's law was obeyed in the concentration range of 0.482-24.077 µg/ml with good correlation coefficient (R^2= 0.9996). The relative standard deviation did not exceed 2.8%. The limit of detection (LOD) and the limit of quantification (LOQ) were 0.045 and 0.13 µg/ml, respectively. No interferences were caused by excipients, aspirin (ASP) and fenofibrate (FEN), but Ezetimibe (EZE), clopidogrel (CP), telmisartan (TEL), glimepiride (GLM) and diltiazem (DIL), interfere.

Conclusion: The developed method is applicable for the determination of rosuvastatin in pure and different dosage forms with an average recovery of 96.0 to 105.0% and the results are in good agreement with those obtained by the RP-HPLC reference methods.

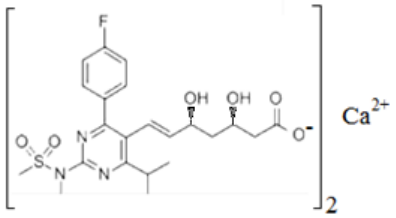
Keywords: Direct spectrophotometric method, Rosuvastatin, Bromocresol green, Ion-pair complex.

INTRODUCTION

Rosuvastatin calcium $(C_{22}H_{27}FN_3O_6S)_2Ca$, mol. mass 1001.14 g, is a synthetic lipid lowering agent which belongs to the drug class known as statins. It is widely used to treat hypercholesterolemia and prevent cardiovascular diseases. It is the calcium salt of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl (methyl sulfonyl) amino] pyrimidin-5-yl] (3R, 5S)-3,5-di hydroxyhept-6-enoic acid, while rosuvastatin (RSV) is $C_{22}H_{28}FN_3O_6S$ and its mol. mass is 481.539 g, see scheme 1. Rosuvastatin calcium is a white amorphous powder slightly soluble in water, freely soluble in methanol, ethanol, chloroform, DMSO and DMF [1-4].



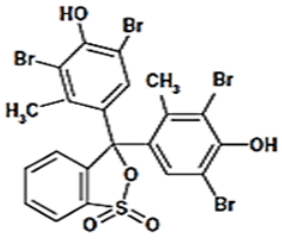
Rosuvastatin $C_{22}H_{28}FN_3O_6S$, RSV



Rosuvastatin calcium $(C_{22}H_{27}FN_3O_6S)_2Ca$, RSVCa

Scheme 1: Chemical structure of rosuvastatin and rosuvastatin calcium

Bromocresol green $(C_{21}H_{14}Br_4O_5S)$, mol. mass 698.01 g, is a dye of the triphenylmethane family (triarylmethane dyes), see scheme 2 [5].



Scheme 2: Chemical structure of bromocresol green $(C_{21}H_{14}Br_4O_5S)$

Various spectrophotometric [6-40], HPLC [41-43], capillary zone electrophoresis [44] and electrochemical methods [45-47] have been reported for the determination of rosuvastatin calcium in pure as well as in dosage forms. Spectrophotometric methods based on complex formation were successfully applied for the determination of rosuvastatin directly or by extraction [6-13].

A simple, sensitive and economical spectrophotometric method is developed for the determination of rosuvastatin calcium RSV_{Ca} in pure form and its pharmaceutical formulations in acetonitrile. This method is based on the oxidation of rosuvastatin calcium by iodine and formation triiodide (I_3^-) complex. The formed complex was measured at 291 and 360 nm against the reagent blank prepared in the same manner. The optimum experimental parameters are selected. Beer's law is valid within a concentration range of 2.408-48.154 µg/ml. The developed method is applied for the determination of rosuvastatin calcium in pure and its

pharmaceutical formulations without any interference from excipients with an average recovery of 95.8 to 104.0% [6].

A simple and sensitive visible direct spectrophotometric method has been developed for the estimation of rosuvastatin calcium in bulk and pharmaceutical dosage forms. This method is based on the reaction of RSV_{Ca} with 3-methyl 1,2 benzthiazoline hydrazide hydrochloride reagent (MBTH) in presence of ferric chloride solution, to produce a green color (λ_{max} 631 nm). Beer's law was obeyed in the concentration range of 5–30 µg/ml [7].

Simple and sensitive direct spectrophotometric methods were also developed for the estimation of rosuvastatin in bulk and pharmaceutical dosage forms. The first method is based on oxidation followed by complex formation of the drug with chloralinic acid (λ_{max} 530 nm) and the second method is based on oxidation followed by complex formation of the drug with potassium permanganate (λ_{max} 410 nm). Beer's law was obeyed in the concentration ranges 1-3 µg/ml and 0.25-1.25 µg/ml for two methods, respectively [8].

A sensitive and rapid extractive spectrophotometric method has been developed for the assay of rosuvastatin calcium (RSV_{Ca}) in pharmaceutical formulations. The method is based on the formation of ion-pair complex with Safranin (SFN) in phosphate buffer at pH 7.2. The complex was extracted into chloroform then measured at 518 nm. Beer's law was obeyed in the concentration range of 5-25 µg/ml. Limit of detection and Limit of quantification for rosuvastatin calcium were found to be 1.5 µg/ml and 2.5 µg/ml, respectively [9].

Two simple extractive Spectrophotometric methods are described for the determination of rosuvastatin calcium (RSV_{Ca}) in pure form and in pharmaceutical formulations. These methods are based on the formation of ion association complexes of the RSV with basic dyes safranin O (Method A) and methylene blue (Method B) in basic buffer of pH 9.8 followed by their extraction in chloroform. The absorbance of the chloroform layer for each method was measured at its appropriate λ_{max} against the reagent blank. Beer's law was obeyed in the concentration range of 5.0–25.0 µg/ml and 2.5–12.5 µg/ml, respectively. These methods have been statistically evaluated and are found to be precise and accurate [10].

Two simple and sensitive methods have been developed for the estimation of rosuvastatin in bulk and in pharmaceutical dosage forms. Method A is based on the oxidative coupling of rosuvastatin with MBTH in the presence of oxidant cerric ammonium sulphate, λ_{max} 658 nm. Method B is based on the formation of co-ordination complex between rosuvastatin and cobalt thiocyanate and the blue colored complex formed is extracted into nitrobenzene, λ_{max} 626 nm. The colored species obeyed Beer's Law in the concentration range 2-14 µg/ml and 50-250 µg/ml for method A and method B respectively. Recovery studies were carried out by the standard addition method. Both the proposed methods were applied for the determination of rosvastatin in bulk and pharmaceutical dosage forms [11].

Simple and accurate spectrophotometric methods are presented for the determination of five 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-CoA) reductase inhibitors (statins), including rosuvastatin, in pharmaceutical preparations based on the reaction of drugs as n-electron donors with 7,7,8,8-tetracyanoquinodimethane as π-acceptors to give highly colored complex species which were extracted by suitable solvent [12].

Most spectrophotometric methods employ ion-pair extraction procedures. In this case, the ion-pair complex was extracted into an organic solvent, which is immiscible with water, and the concentration of the resulting ion pair in the organic phase is determined spectrophotometrically. The ion-pair extraction technique has some difficulties and inaccuracies due to incomplete extraction or the formation of emulsions between the hydrocarbon solvent and the basic compound-containing solution. In response to the problems resulting from extraction of the ion-pair complex, it is better to determine formed ion pair complex without extraction [48]. In this study, extraction-free spectrophotometric method for determination of RSV was developed.

MATERIALS AND METHODS

Instruments and apparatus

Spectrophotometric measurements were made in Spectro Scan 80 DV UV-VIS Spectrophotometr with 0.2 cm and 1 cm quartz cells. An ultrasonic processor model POWERSONIC 405 was used to sonicate the sample solutions. The diluter pipette model DIP-1 (Shimadzu), having 100 µl sample syringes and five continuously adjustable pipettes covering a volume range from 20 to 5000 µl (model PIPTMAN P, GILSON).

Centrifuge (Centurion Scientific Ltd., Model: K2080-Manufactured in the United Kingdom) was used for preparation of the experimental solutions. SARTORIUS TE64 electronic balance was used for weighing the samples.

Reagents

Rosuvastatin calcium (98.6%) was supplied by BDR PHARMACEUTICALS INTERNATIONAL PVT. LTD. (INDIA), its purity as rosuvastatin was 94.66%. Aspirin, fenofibrate, Ezetimibe, clopidogrel, telmisartan, glimepiride and diltiazem were obtained as gift sample from ASIA, BARAKAT, BAHRI, DIAMOND and UNIPHARMA Co. in Syria. Bromocresol green (97%) of analytical grade and chloroform extra pure was from MERCK. All solvents and reagents were analytical grade chemicals.

Stock standard solution of bromocresol green ($1x10^{-3}$ mol/l)

Accurately weighed 35.98 mg of BCG was dissolved in chloroform into the volumetric flask (50 ml) and diluted up to mark with chloroform.

Stock standard solution of rosuvastatin ($1x10^{-4}$ mol/l)

This solution was prepared by dissolving 25.38 mg of (RSV_{Ca}) in chloroform then diluting to 50 ml with chloroform, $1x10^{-3}$ mol/l of RSV (a), then diluting 5.000 ml from this solution to 50 ml with chloroform, $1x10^{-4}$ mol/l of RSV (b).

Working standard solutions of rosuvastatin

The stock solution was further diluted daily just before the use to obtain working solutions of RSV in the concentrations: 1, 2, 4, 6, 8, 10, 20, 30, 40 and 50 µM (0.482, 0.963, 1.926, 2.889, 3.852, 4.815, 9.631, 14.446, 19.262 and 24.077 µg/ml) by transferring different aliquots from stock standard solution (b): 0.1, 0.2, 0.4, 0.6, 0.8, 1.0, 2.0, 3.0, 4.0 and 5.0 ml into 10 ml volumetric flasks, then 1 ml from stock standard solution of BCG was added, diluted to 10 ml with chloroform.

Sample preparation

Commercial formulations (as tablet) were used for the analysis of rosuvastatin. The pharmaceutical formulations subjected to the analytical procedure were:

(1) *Rosuvastatin* tablets, Balsam pharma Co., Homs–SYRIA (Mfg. 07/2013, Exp. 07/2017), each tablet contains: 5,10,20 and 40 mg of RSV.

(2) *Rosuvastatin-ElSaad* tablets, ELSaad pharma, Aleppo–SYRIA, (Mfg. 04/2012, Exp. 04/2016), Each tablet contains: 5,10,20 and 40 mg of RSV.

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

Stock solutions of pharmaceutical formulations

Ten tablets of each studied pharmaceutical formulation were weighed accurately, crushed to a fine powder and mixed well. An amount of the powder equivalent to the tenth of the weight of one tablet was solved in chloroform using ultrasonic, 10 ml of chloroform was added, filtered over a 50 ml flask and washed by the same solvent, then diluted to 50 ml with chloroform.

This solution contains the follows: 10, 20, 40 and 80 µg/ml of RSV for all studied pharmaceutical formulations contain 5, 10, 20 and 40 mg/tab, respectively.

Working solutions of pharmaceuticals

These solutions were prepared daily by diluting 2.00, 1.00, 0.50 and 0.25 ml from stock solutions of pharmaceutical formulations for contents: 5, 10, 20 and 40 mg/tab, respectively, then adding 1 ml from stock standard solution of BCG and adjusting the volume up to 10 ml with chloroform (each solution contains 2 µg/ml of RSV).

Working standard addition solutions of pharmaceuticals

Aliquots (2.00, 1.00, 0.50 and 0.25 ml) from stock solutions of pharmaceuticals for different dosage forms, respectively, were taken with 0.40, 0.80, 2.00 and 4.00 ml from stock standard solution (b) of RSV, and 1.0 ml from stock standard solution of BCG was added, then diluted to 10 ml with chloroform; these solutions contain 2.000 µg/ml of RSV (from pharmaceuticals) plus 1.926, 3.852, 9.631 and 19.262 µg/ml of standard rosuvastatin, respectively.

Procedure

A solution (10 ml) containing an appropriate concentration of rosuvastatin (or working solutions of pharmaceuticals or working standard addition solutions of pharmaceuticals) with an appropriate amount of bromocresol green in chloroform was ready for spectrophotometric measurement at λ_{max} =416 nm.

RESULTS AND DISCUSSION

The different experimental parameters affecting the spectro photometric determination of rosuvastatin calcium through ion-pair complex formation with bromocreol green in chloroform were studied in order to determine the optimal conditions for the determination of RSV.

Spectrophotometric results

UV-Vis spectra of RSV_{Ca}, BCG, the formed complex BCG: RSV, ASP and FEN solutions (using chloroform as blank) were obtained. RSV_{Ca}, ASP and FEN solutions do not absorb in the range 400-600 nm. Bromocresol green (BCG) solutions have small absorption at 416 nm. BCG: RSV complex solutions have maximum absorption at 416 nm. (see fig. 1).

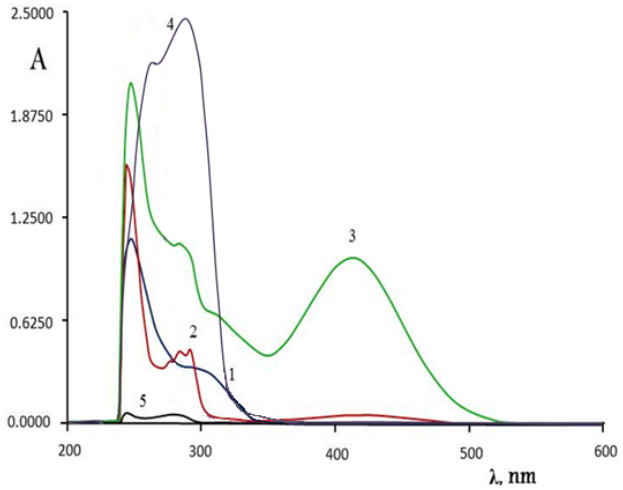


Fig. 1: UV-Vis spectra in chloroform of: 1-5.0x10^{-5} mol/l of RSV; 2-1x10^{-4} mol/lof BCG; 3-5.0x10^{-5} mol/l ion-pair complex (5.0x10^{-5} mol/l of RSV with 1.0x10^{-4} mol/l of BCG); 4-5.0x10^{-5} mol/l of FEN; 5-5.0x10^{-5} mol/l of ASP {blank is chloroform,ℓ =1 cm}

The effect of time and temperature

The effect of time and temperature on the complex formation was studied within the ranges 5-120 min and 15-50^{o}C. It was found that the formed complex wasn't affected by time or temperature at those ranges.

The effect of BCG concentration

The effect of BCG concentration on complex formation was investigated. It was observed that the absorbance of the formed complex increased coinciding with increasing the ratio of C_{BCG}: C_{RSV} until the ratio (1:1), then stayed quasi-constant (the ratio C_{BCG}: C_{RSV} ≥2 was chosen).

Composition of RSV: BCG complex

The composition of RSV: BCG complex was determined by the molar ratio method and Job's method of continuous variation.

Molar ratio method

The stoichiometry of RSV: BCG complex was studied by molar ratio method according to following equation: Amax= f([RSV]/[BCG]). It confirmed that the binding ratio of RSV: BCG complex is equal to (1:1); where the concentration of BCG was constant 50 µM and the concentrations of RSV changed from 0 to 100 µM (fig. 2).

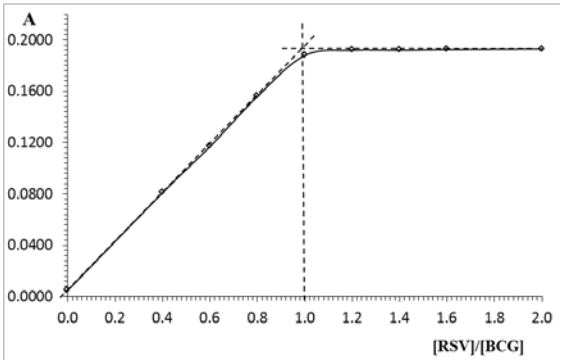


Fig. 2: Molar ratio method to calculate binding ratio of RSV: BCG complex at λ=416 nm ([BCG]= 50 µM, blank is chloroform, ℓ =0.2 cm)

Job's method of continuous variation

Continuous variation was utilized to check the composition of RSV: BCG complex. The absorbance of the complex was plotted against the mole fraction [RSV]/[RSV]+[BCG]. The plot reached maximum value at a mole fraction of 0.5 (fig. 3). This indicated complex formation (RSV: BCG) in the ratio of 1:1.

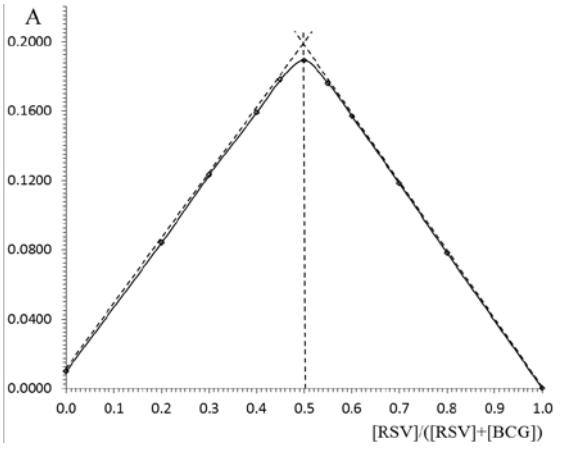


Fig. 3: Job's method of continuous variation to calculate binding ratio of RSV: BCG complex at λ=416 nm ([BCG]+[RSV]=100 µM, blank is chloroform, ℓ =0.2 cm)

The optimum conditions for spectrophotometric determination of rosuvastatin through ion-pair complex formation using bromocresol green in chloroform were shown in table 1.

Table 1: The optimum conditions for spectrophotometric determination of RSV by complex formation with BCG in chloroform

Parameters	Operating modes
Temperature of solution	25±5°C
C_{BCG}: C_{RSV}, M	≥2
Solvent	chloroform
Stability (h)	24
λ_{max} of RSV: BCG complex	416 nm
Molar absorptivity of RSV: BCG complex (ε)	$1.92x10^4$ l. mol^{-1}. cm^{-1}
Light path (ℓ)	0.2 and 1.0 cm
Spectra range	200–600 nm
Working $C_{BCG,}$ mol/l	$1x10^{-4}$ (100 µM)

Mechanism of reaction

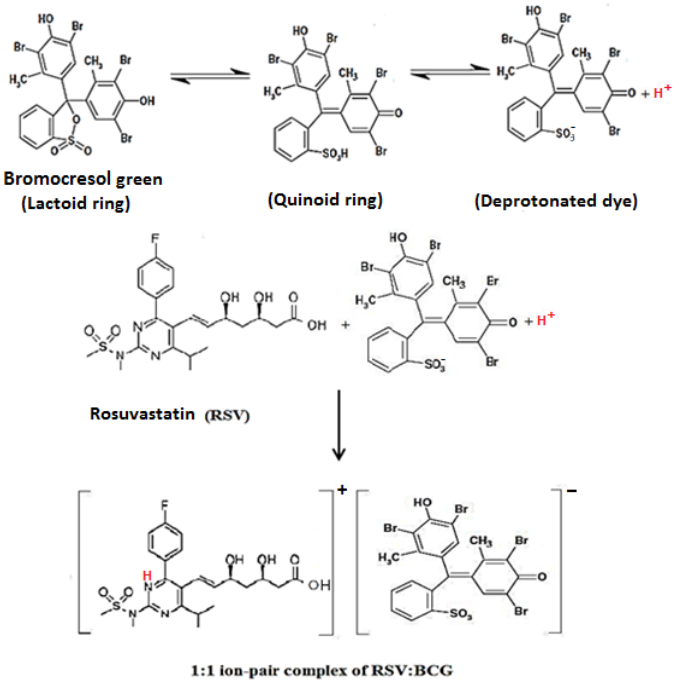
Anionic dyes such as BCG form ion-pair complexes with the positively charged nitrogen-containing molecule.

The colour of such dyes is due to the opening of lactoid ring and subsequent formation of quinoid group (deprotonated). Rosuvastatin is protonated and forms ion-pair with the dye. Each drug-dye complex with two oppositely charged ions (positive on the drug and negative on the dye) behaves as a single unit held together by an electrostatic binding [47-49]. The suggested mechanism of RSV-BCG ion-pair complex formation is shown in Scheme 3.

Calibration curve

The calibration curve of RSV in pure form through complexation with BCG showed excellent linearity over concentration range of 1.0-50.0 µM (0.482–24.077 µg/ml), (fig. 4 and 5).

The spectra characteristics of the method such as the molar absorptivity (ε), $\lambda_{max,}$ Beer's law, regression equation {at λ_{max}= 416 nm (y=a. x+b); where y=absorbance, a=slope, x=concentration of RSV in µM or µg/ml,b=intercept} the correlation coefficient, limit of detection (LOD) and limit of quantification (LOQ) are summarized in table 1 and 2.



Scheme 3: Mechanism of RSV: BCG complex formation

Analytical results

Spectrophotometric determination of RSV through complexation with BCG in chloroform within optimal conditions using the calibration curve was applied. The results, summarized in table 3, showed that the determined concentration of RSV was rectilinear over the range of 1.0 to 50.0 µM or 0.482 to 24.077 µg/ml with relative standard deviation (RSD) not more than 2.8%. The limit of detection (LOD) and limit of quantification (LOQ) was found to be 0.092 and 0.28 for C_{RSV} by µM and 0.045 and 0.13 for C_{RSV} by µg/ml, respectively. The results obtained from the developed method have been compared with the official RP-HPLC method [42] and good agreement was observed between them.

Precision and accuracy

The precision and accuracy of proposed method was checked by recovery study by an addition of standard drug solution to pre-analyzed sample solution at three different concentration levels (80%, 100% and 120%) within the range of linearity for RSV. The basic concentration level of sample solution selected for spiking of the RSV standard solution was 10 µg/ml. The proposed method was validated statistically and through recovery studies, and was successfully applied for the determination of RSV in pure and dosage forms with percent recoveries ranged from 98.4% to 100.1%.

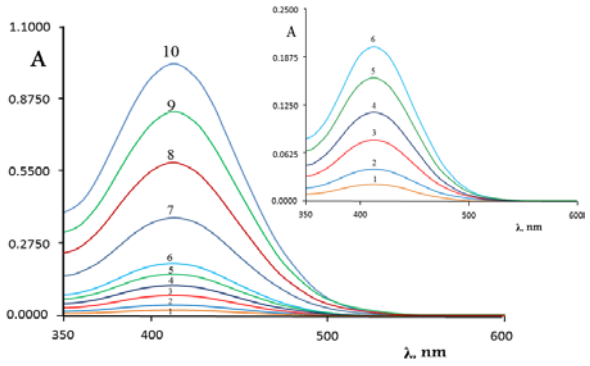


Fig. 4: Spectra of BCG (1×10^{-4} M) with RSV; where C_{RSV} as the follows: 1-0.482; 2-0.963; 3-1.926; 4-2.889; 5-3.852; 6-4.815;7-9.631; 8-14.446; 9-19.262; 10-24.077 µg/ml {Blank is BCG solution $1x10^{-4}$M in chloroform; ℓ = 1 cm}

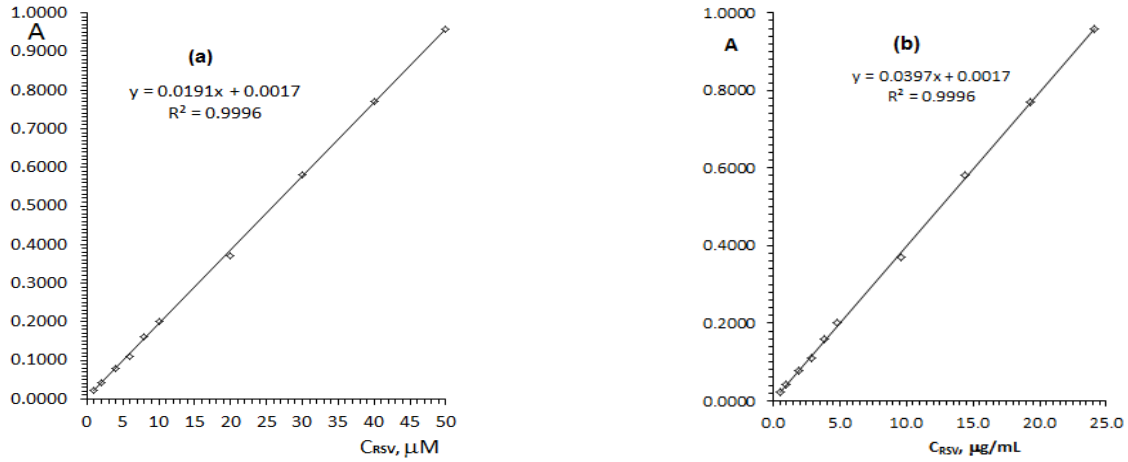


Fig. 5: Calibration curve for determination of RSV according to optimal conditions at λ_{max}: 416 nm C_{RSV}: 1.0, 2.0, 4.0, 6.0, 8.0, 10.0, 20.0, 30.0, 40.0 and 50.0 µM (a) and 0.482, 0.963, 1.926, 2.889, 3.852, 4.815, 9.631, 14.446, 19.262 and 24.077 µg/ml (b) (Blank is BCG solution $1x10^{-4}$ M in chloroform, ℓ = 1 cm)

Table 2: The parameters established for spectrophotometric determination of RSV by complex formation with BCG in chloroform.

Parameters	Operating values
Regression equation at λ_{max}=416 nm for C_{RSV} by µM:	
Slope	0.0191
Intercept	0.0017
Correlation coefficient (R^2)	0.9996
Regression equation at λ_{max}=416 nm for C_{RSV} by µg/ml:	
Slope	0.0397
Intercept	0.0017
Correlation coefficient (R^2)	0.9996
Beer's Law Limit, for C_{RSV} by µM	1.0–50.0
Beer's Law Limit, for C_{RSV} by µg/ml	0.482–24.077
RSD%	2.8
LOD(3.3SD), for C_{RSV} by µM	0.092
LOQ (10SD), for C_{RSV} by µM	0.28
LOD(3.3SD), for C_{RSV} by µg/ml	0.045
LOQ (10SD), for C_{RSV} by µg/ml	0.13

n=5, t=2.776.

Table 3: Spectrophotometric determination of RSV through complex formation with BCG within optimal conditions using calibration curve in chloroform

X_i, µg/ml (taken)	$*\overline{X}$, µg/ml (found)	SD, µg/ml	$\frac{SD}{\sqrt{n}}$, µg/ml	$\bar{x} \pm \frac{t.SD}{\sqrt{n}}$ µg/ml	RSD %	$\overline{X}$, µg/ml RP-HPLC [42]
0.482	0.486	0.014	0.0061	0.486±0.017	2.8	0.484
0.963	0.965	0.026	0.012	0.965±0.032	2.7	0.961
1.926	1.947	0.051	0.023	1.947±0.063	2.6	1.930
2.889	2.829	0.074	0.033	2.829±0.091	2.6	2.890
3.852	3.962	0.107	0.048	3.962±0.133	2.7	3.942
4.815	4.970	0.129	0.058	4.970±0.160	2.6	4.861
9.631	9.352	0.224	0.100	9.352±0.279	2.4	9.630
14.446	14.516	0.319	0.143	14.516±0.396	2.2	14.410
19.262	19.327	0.406	0.182	19.327±0.504	2.1	19.301
24.077	24.063	0.481	0.215	24.063±0.597	2.0	24.080

* n=5, t= 2.776

Repeatability

The repeatability was evaluated by performing 10 repeat measurements for 1.926 µg/ml of RSV using the studied spectrophotometric method under the optimum conditions. The found amount of RSV ($\bar{x}$ ±SD) was 1.947±0.051 µg/ml and the percentage recovery was found to be 101.1±2.6 with RSD of 0.026. These values indicate that the proposed method has high repeatability for RSV analysis.

Application

The developed spectrophotometric method was applied to determine rosuvastatin in some pharmaceutical preparations through complex formation by BCG in chloroform according to the

optimal conditions. Regression equations and correlation coefficients were included in table 4. Standard addition curves were used for the determination of rosuvastatin in different pharmaceutical preparations.

The amount (m) of rosuvastatin in one tablet was calculated from the following relationship: m = h. m', where: m' is the amount of RSV in tablet calculated according to the following regression equation: y=a. x+b; when y=0; m'=x=b/a=intercept/slope (µg/ml), h conversion factor is equal to 2.5, 5, 10 and 20 for 5, 10, 20 and 40 mg/tab of RSV. The results of quantitative analysis for RSV in some pharmaceutical preparations, calculated using the standard additions method, were summarized in Tables 5. Some pharmaceutical preparations of RSV contain another drug like ASP, FEN, EZE, CP, TEL, GLM and DIL in combined with rosuvastastin. It was found that neither ASP nor FEN reacts with BCG, so they don't form complex with the dye, while the other drugs react with the dye.

The proposed method was simple, direct, specific and successfully applied to the determination of RSV in mentioned pharmaceuticals without any interference from excipients, ASP and FEN. Average recovery ranged between 96.0 to 105.0%. The results obtained by this method agree well with the contents stated on the labels and were validated by RP-HPLC [42].

Table 4: Regression equations and correlation coefficients for determination of RSV in some pharmaceutical preparations using developed spectrophotometric method at λ_{max}=416 nm

Commercial name	Content of RSV mg/tab.	m'(RSV), µg/ml	Regression equations*	Correlation coefficients	Amount of RSV (m), mg/tab.
Rosuvastatin	5	1.961	y=0.0395x+0.0774	R^2=0.9992	$m_{AT/tab.}$=2.5m'=4.90
	10	2.016	y=0.0399x+0.0804	R^2=0.9993	$m_{AT/tab.}$=5m'=10.08
	20	2.064	y=0.0398x+0.0821	R^2=0.9994	$m_{AT/tab.}$=10m'=20.63
	40	2.050	y=0.0392x+0.0804	R^2=0.9996	$m_{AT/tab.}$=20m'=40.40
Rosuvastatin-Elsaad	5	1.920	y=0.0391x+0.0751	R^2=0.9993	$m_{AT/tab.}$=2.5m'=4.80
	10	1.998	y=0.0397x+0.0793	R^2=0.9993	$m_{AT/tab.}$=5m'=9.97
	20	2.100	y=0.0394x+0.0827	R^2=0.9995	$m_{AT/tab.}$=10m'=21.00
	40	2.062	y=0.0398x+0.0821	R^2=0.9996	$m_{AT/tab.}$=20m'=41.24
Turbovas	10	2.004	y=0.0395x+0.0792	R^2=0.9994	$m_{AT/tab.}$=5m'=10.02
	20	2.036	y=0.0399x+0.0812	R^2=0.9995	$m_{AT/tab.}$=10m'=20.36

*y= n A, x= concentration of Rosuvastatin (µg/ml)= m' = intercept/slope.

Table 5: Determination of RSV in some Syrian pharmaceutical preparations using spectrophotometric method through complex formation with BCG in chloroform, λ_{max}=416 nm

Commercial name	Contents, RSV mg/tab.	*$\bar{x}$, mg/tab.	RSD%	Recovery %	$\bar{x}$, (Recovery %) RP-HPLC [42]
Rosuvastatin	5	4.90	3.8	98.0	98.4
	10	10.08	3.7	100.8	100.6
	20	20.64	3.6	103.2	103.4
	40	40.40	3.6	101.0	100.8
Rosuvastatin-Elsaad	5	4.80	3.9	96.0	96.5
	10	9.97	3.7	99.7	99.8
	20	21.00	3.6	105.0	104.7
	40	41.24	3.5	103.1	103.0
Turbovas	10	10.02	3.7	100.2	100.5
	20	20.36	3.6	101.8	102.0

* n=5

Interference

Some drugs as ASP, FEN, EZE, CP, TEL, GLM and DIL exist in combined with rosuvastatin in some pharmaceutical formulations. ASP, FEN and tablet fillers (excipients) such as lactose, starch, stearic acid, preservations and bacteriostatics while used in parental preparations don't interfere in this method. EZE, CP, TEL, GLM and DIL, interfere.

CONCLUSION

The developed spectrophotometric method is simple, direct (extraction-free), cost-effective and specific for the determination of rosuvastatin in pure and its pharmaceutical formulations.

This method is based on the formation of ion-pair complex between rosuvastatin and bromocresol green in chloroform (λ_{max} =416 nm).

Beer's law in the optimum experimental conditions is valid within a concentration range of 0.482-24.077 µg/ml. The developed method is applied for the determination of rosuvastatin in pure and its commercial tablets without any interference from excipients, aspirine and fenofibrate with an average recovery of 96.0 to 105.0%.

CONFLICT OF INTERESTS

The authors have declared that no conflict of interests exists.

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