



Scholars Research Library

Der Pharmacia Lettre, 2012, 4 (4):1054-1059
(<http://scholarsresearchlibrary.com/archive.html>)



Q-Absorbance and Multicomponent UV - Spectrophotometric Methods for Simultaneous Estimation of Rosuvastatin calcium and Fenofibrate in Pharmaceutical Formulation

Prashant S. Mandwal*, Pratik R. Patel, Kapil M. Agarwal, Sanjay J. Surana

R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur Dist: Dhule

ABSTRACT

Two simple UV-Spectrophotometric methods have been developed for simultaneous determination of Rosuvastatin calcium and Fenofibrate in pharmaceutical formulation. Methanol AR grade was used as solvent. In Method-I (Q-absorbance absorbance ratio) involves formation of Q-absorbance equation at two wavelengths i.e. 255.99 nm (isoabsorptive point) and 286 nm (λ max of Fenofibrate). While, in Method-II (Multicomponent Mode of Analysis) involves the measurement of absorbance at two wavelengths i.e. 243 nm, λ max of Rosuvastatin calcium and 286 nm, λ max of Fenofibrate. In both methods, Rosuvastatin calcium and Fenofibrate followed same linearity range at the concentration of 03 - 18 μ g/ml at their respective λ max. Both these methods were found to be accurate, precise and rugged as indicated by low values of % RSD. Both these methods were also found to be rapid and economical can successfully be applied for the routine analysis of bulk and combined tablet dosage form.

Keywords: Rosuvastatin calcium, Fenofibrate, Q-Absorbance ratio method, Multicomponent mode of analysis, Pharmaceutical formulation.

INTRODUCTION

Rosuvastatin calcium (ROS) is chemically (E)-(3R,5S)-7-{4-(4-fluorophenyl)-6-isopropyl-2-{methyl(methylsulphonylamino)pyrimidine-5-yl}-3,5-dihydroxyhepten-6-oic acid calcium. ROS belongs to statin class of drugs used to treat hypercholesterolemia both in patients with established cardiovascular disease as well as those who are at a high risk of developing atherosclerosis. These drugs inhibit the rate limiting key enzyme known as 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase involved in cholesterol biosynthesis. Statins cause reduction in low density lipoproteins-C (LDL-C), total cholesterol (TC) and triglycerides (TG) and elevation in high-density lipoprotein-C (HDL-C) [1, 2]. Fenofibrate (FEN) chemically Propan - 2 - yl 2 - [4 - (4 - chlorobenzoyl) phenoxy] - 2 - methyl propionate is the lipid regulating drug. FEN increases lipolysis and elimination of triglyceride-rich particles from plasma by activating *lipoprotein lipase* and reducing production of apoprotein C-III (an inhibitor of *lipoprotein lipase* activity) [2 - 4]. The structure of both drugs were shown in **fig. 1**

A detailed survey of analytical literature for estimation of ROS revealed several methods based on varied techniques viz, HPLC [5-8], Capillary Zone Electrophoresis [9], Spectrophotometry [10] and High Performance Thin Layer Chromatography (HPTLC) [11]. Estimation of FEN were also reported in bulk and formulations using HPLC [12], Spectrophotometry [13] HPTLC [14, 15] and some analytical methods reported on this combination using UV [16] HPLC [17].

Form literature survey reveals that no simultaneous estimation of both drugs in their combined dosage form. In the present work, an endeavor has been made to estimate both drugs simultaneously by Q - absorbance ratio method and

Multicomponent mode of analysis. Further, methods were validated for precision, accuracy and ruggedness as per ICH guideline [18].

MATERIALS AND METHODS

Chemicals

Rosuvastatin calcium and Fenofibrate was obtained as a gift samples by Glenmark, Nasik, Maharashtra, India. Methanol (A.R. Grade) was purchased from E. Merck Ltd., Mumbai, India. The commercial fixed dose combination of ROS and FEN (10:67 mg tablet) was procured from local market.

Instrumentation

UV-Visible spectrophotometer (Shimadzu 2450 with UV Probe 2.21 software and Shimadzu- 1602 for 'Q absorbance ratio method' and 'Multicomponent mode of analysis', respectively)

Selection of common solvent

Methanol of analytical reagent grade was selected as common solvent for developing spectral characteristics of drug. The choice of the solvent was made after evaluating the solubility in different solvents and as per literature survey.

Preparation of Stock standard solutions

Stock solutions of ROS and FEN were prepared separately by dissolving 10 mg in 100 mL methanol to obtained 100 µg/mL concentrations. These stock solutions, worked as standard solutions having concentration at 10 µg/mL for ROS and 10 µg/mL for FEN.

They were scanned in the UV- region i.e. 400 - 200 nm. The overlay spectrum (**fig.2**) was obtained to determine the maximum absorbance (λ max) and iso-absorptive point.

Study of linearity curves

An appropriate volume of ROS and FEN in the range of 0.3-1.8 mL transferred into series of separate 10 mL volumetric flasks and volume was made up to mark with methanol to get concentrations in the range of 03 – 18 µg/mL for both drugs respectively. The absorbance of these drugs was measured at 243 and 286 nm respectively and calibration curves was plotted as concentrations *versus* absorbances.

EXPERIMENTAL

Method – I (Q-Absorbance Ratio)

Q-Absorbance method uses the ratio of absorbance at two selected wavelengths, one at isoabsorptive point and other being the λ max of one of the two drugs. ROS and FEN have λ max at 243 and 286 nm respectively and iso-absorptive point 255.99 nm. The wavelengths selected for analysis were 286 and 255.99 nm, respectively. E (1%, 1cm) values of ROS and FEN were determined at 286 and 255.99 nm.

The concentration of two drugs in mixture was calculated by using following equations:

$$C_{ROS} = \frac{Q_m - Q_y}{Q_x - Q_y} \times \frac{A}{ax1} \quad (1)$$

$$C_{FEN} = \frac{Q_m - Q_x}{Q_y - Q_x} \times \frac{A}{ay1} \quad (2)$$

Where,

$$Q_m = \frac{\text{Absorbance of sample at 286.0 nm}}{\text{Absorbance of sample at 255.99 nm}}$$

$$Q_x = \frac{E(1\% \text{ 1cm}) \text{ of ROS at 286.0 nm}}{E(1\% \text{ 1cm}) \text{ of ROS at 255.99 nm}}$$

$$Q_y = \frac{E(1\% \text{ 1cm}) \text{ of FEN at } 286.0 \text{ nm}}{E(1\% \text{ 1cm}) \text{ of FEN at } 255.99 \text{ nm}}$$

'A' is the absorbance of mixture at 255.99 nm and ax1 (429.6), ax2 (196.0) and ay1 (429.86), ay2 (536.36) are absorptivities E (1%, 1 cm) of ROS and FEN at 255.99 nm and 286 nm and Qm= A2/A1, Qy = ay2/ay1 and Qx = ax2/ax1.

Method – II (Multicomponent mode of analysis)

Six mixed standard solutions of ROS and FEN in the ratio of 1:1 µg/mL were prepared in methanol. All the standard solutions were scanned over the range of 400 - 200 nm, in the multicomponent mode, using two sampling wavelength 243 nm (λ max of ROS) and 286 nm (λ max of FEN). The overlay spectra of mix standard solution shown in **fig. 3**. The data from these scans were used to determine the concentrations of two drugs in tablet sample solutions.

Analysis of tablet Formulation

The content of twenty tablets (Rozel F) were accurately weighed and crushed into fine powdered. A quantity of powder equivalent to 10.44 mg of ROS and 70 mg of FEN was transferred into 100 mL volumetric flask containing 60 mL methanol and 6ml of ROS stock solution was added (standard addition method), shaken manually for 20 min and the volume was made up to the mark and filtered through Whatmann filter paper (no.41). The solution was further diluted with methanol to give the concentration within Beer & lembert's law. Absorbance of this solution was measured at 255.99 nm and 286 nm and concentrations of these two drugs in the sample was calculated using equation (1) and equation (2) (Method I). The same sample solutions were subjected to analysis in the multi component mode of instrument (UV - Spectrophotometer 1602). The solution was scanned over the wavelength range of 400 - 200 nm and the concentration of each drug were determined by analysis of spectral information of the sample solution with reference to the mixed standards (Method II). The analysis procedure was repeated six times with tablet formulations. The results of analysis were reported in **Table- 1**.

RESULTS AND DISCUSSION

In methanol, ROS and FEN obeyed linearity in the concentration range of 03 - 18 µg/ml for both drugs respectively at their respective λ max with correlation coefficient ($r^2 > 0.99$) in both the case. Marketed brand of tablet were analyzed. The amounts of ROS and FEN determined by 'Method I' was found to be 100.56 and 100.45, respectively; while, by 'Method II', it was found to be 100.87 and 101.57 respectively. In both these methods precision was studied as repeatability (% RSD < 2) and inter and intra-day variations (%RSD < 2) for both drugs. The accuracy of method was determined by calculating mean percentage recovery. It was determined at 80,100 and 120 % level. The ruggedness of the methods was studied by two different analysts using the same operational and environmental conditions. The % recovery, repeatability data, ruggedness data were presented in **Table-2**.

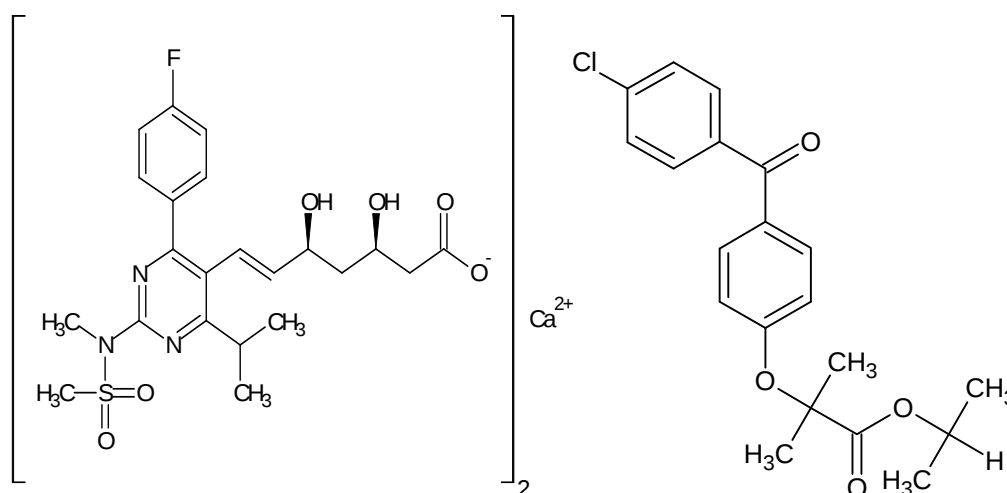


Fig. 1 Chemical structures of Rosuvastatin calcium and Fenofibrate.

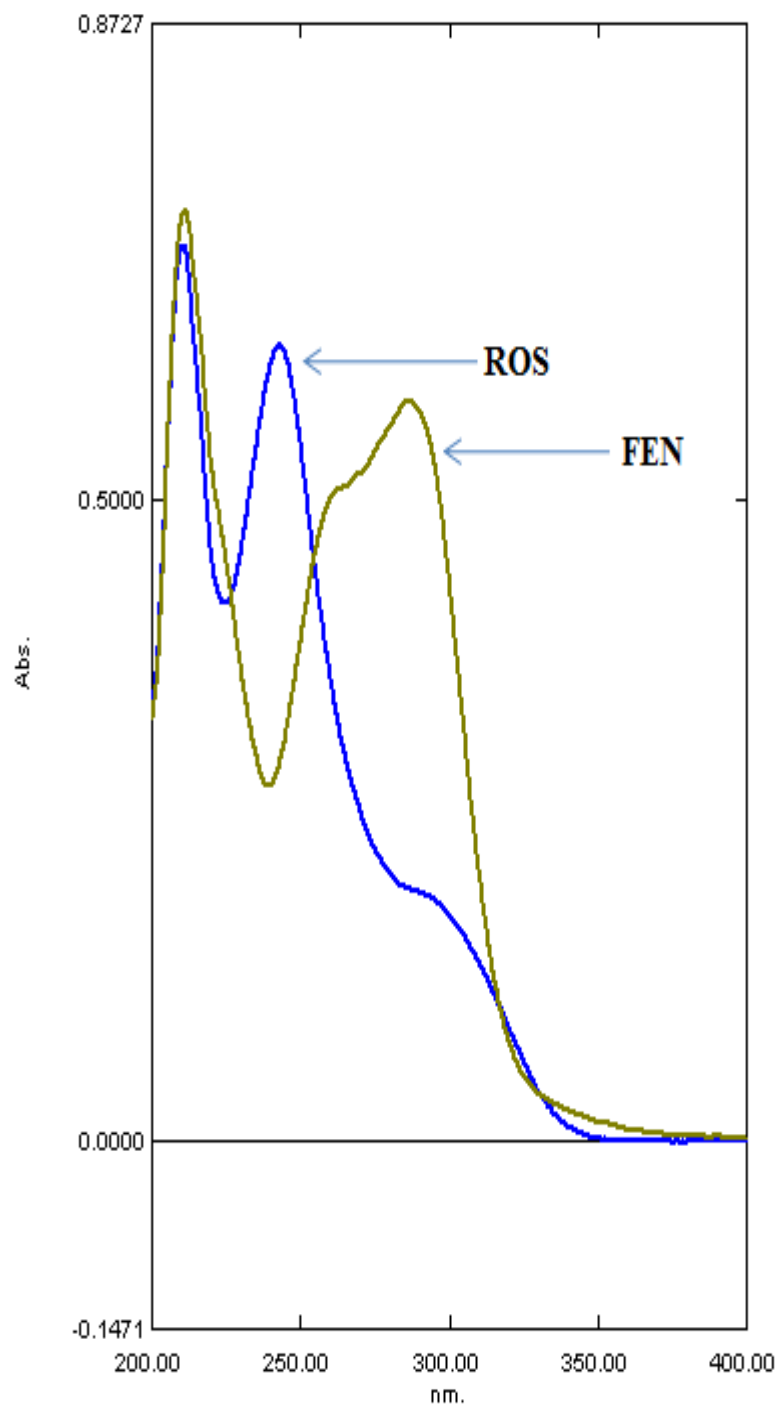


Fig. 2 Overlay spectra of ROS (10mg/mL) and FEN (10mg/mL)

Table 1: Results of simultaneous estimation of marketed formulation (Rozel F) for Method I and II

Method	Drug	Label claim mg/tab	% Label Amount	%RSD
I	ROS	10	100.56	0.442
	FEN	67	100.45	0.452
II	ROS	10	100.87	0.852
	FEN	67	100.57	0.758

Table 2: Validation Parameters

Parameter	Method III		Method IV	
	ROS	FEN	ROS	FEN
Working Wavelengths	243	286	243	286
Linearity range ($\mu\text{g/mL}$)	03 - 18	03 - 18	03 - 18	03 - 18
Precision [%RSD]				
Inter-day [n = 3]	0.26 - 1.27	0.27 - 1.20	0.11 - 1.68	0.18 - 1.98
Intra-day [n = 3]	0.07 - 0.64	0.06 - 0.70	0.09 - 0.64	0.13 - 0.87
Repeatability [n = 6]	0.43	0.49	0.63	0.79
Ruggedness [%RSD]				
Analyst I [n = 6]	0.68	0.68	0.75	0.93
Analyst II [n = 6]	0.71	0.70	0.85	0.53
% Recovery [n = 3]				
%RSD	0.35 - 0.88	0.31 - 0.84	0.92 - 1.35	0.96 - 1.48

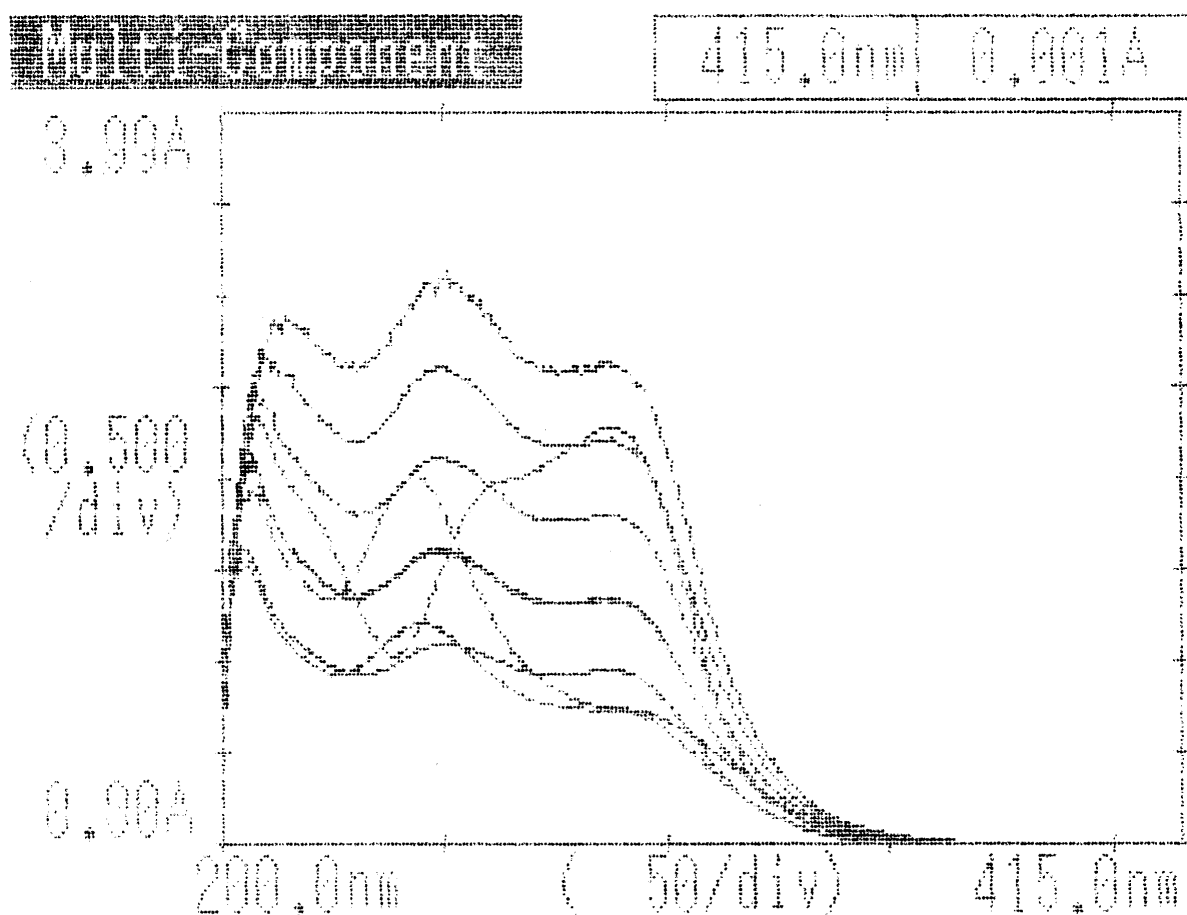


Fig. 3 Overlay spectra mixed standard solutions of ROS and FEN (Multicomponent mode)

CONCLUSION

Both developed methods were found to be accurate, precise and rugged. Further, the developed methods are simple and can usually be used for estimation of both these drugs in their combined dosage form. These UV methods are applicable and overcome the drawbacks of other methods which are very costly. Both methods are used for routine analysis of drugs in bulk and pharmaceutical formulation.

Acknowledgement

The authors wish to thank, Management, R.C. Patel Institute of Pharmaceutical Education and Research, Shirpur, for providing necessary laboratory facilities. Words of gratitude are also expressed for Glenmark Pharmaceuticals Ltd., Nasik, India for providing gift samples as bulk drugs.

REFERENCES

- [1] Indian Pharmacopoeia, Indian Pharmacopoeial Commission, Published by the controller of publication Gaziabad, **2010**, 2071.
- [2] Martindale, The Complete drug reference. Pharmaceutical Press, **2006**, 35, 1154, 1249.
- [3] The Merck Index, An encyclopedia of chemicals, drugs and biological, Merck and Co.,**1996**, 14, 3978.
- [4] British Pharmacopoeia, British Pharmacopoeia Commission Secretariat of the Medicines and Healthcare products Regulatory Agency, Stationary Office, London, **2004**, 811-813.
- [5] T. R. Kumar, N. R. Shitut, P. K. Kumar, M.C. Vinu, V. V. Kumar, R. Mullangi, N. R. Srinivas, *Biomed Chromatogr.*, **2006**, 881-887.
- [6] S. Vittal, T. R. Kumar, N. R. Shitut, M. C. Vinu, V. V. Kumar, R. Mullangi, *Biomed Chromatogr.*, **2006**, 20, 1252-1259.
- [7] D. H. Xu, Z. R. Ruan, Q. Zhou, H. Yuan, B. Jiang, *Rapid Commun Mass Spectrom.*, **2006**, 20, 2369-2375.
- [8] T. N. Mehta, A. K. Patel, G. M. Kulkarni, G. Suubbaiah, *J AOAC Int.*, **2005**, 88, 1142-1147.
- [9] I. Suslu, M. Celebie, S. Altnoz, *Chromatographi.*, **2007**, 66, 65-72.
- [10] B. Uyar, M. Celebier, S. Altinoz, *Pharmazie*, **2007**, 62, 411- 413.
- [11] R. T. Sane, S. S. Kamat, S. N. Menon, S. R. Inamdar, M. R. Mote, *J Planar Chromatogr*, **2007**, 18, 194-198.
- [12] S. M. Fathy, N. I. Mohamed, S. K. Mohie, A. M. Khalid, Y. K. Mohamed, *AJAC.*, **2011**, 3, 332-343.
- [13] S. V. Kutty, S. C. Eapen, S. Mohammed, P. P. Faizal *International Journal of Pharmaceutical Sciences and Drug Research*, **2012**, 4, 74-76.
- [14] C. R. Macwana, *J. Liq Chroma Rel Techno.*, **2012**, 35, 524-532.
- [15] A. A. Shirkhedkar, S. J. Surana, *J Planar Chromatogr.*, **2009**, 5, 355-358.
- [16] R. K. Trivedi, R. R. Kallem, R. Mullang, N. R. Srinivas, *J Pharm Biomed Anal.*, **2005**, 39, 661-669.
- [17] A. Karunakaran, S. Vesta, J. Muthuvijayan, R. Chinthala, *S. J. Pharm. Sci.*, **2011**, 4, 58-63.
- [18] ICH harmonised tripartite guideline, International Conference on Harmonization, IFPMA Geneva **2003**.