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UV Spectrophotometric estimation of Rosuvastatin Calcium and Fenofibrate in bulk Drug and Dosage Form using Simultaneous Equation Method

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Abstract: Rosuvastatin-fenofibrate combination is widely used in the treatment of hypercholesterolemia and hypertriglyceridemia .A new, simple and sensitive spectrophotometric method in ultraviolet region has been developed for the determination of rosuvastatin calcium and fenofibrate in bulk and in pharmaceutical formulations. The drug obeyed the Beer's law [for rosuvastatin concentration range 1-10µg/ml and for fenofibrate concentration range2-20µg/ml] and showed good correlation. The result of analysis was validated by recovery studies. The method was found to be simple, accurate, precise, economical and robust. In this method, there is no interference from any common pharmaceutical additives and diluents.
Keywords: Rosuvastatin, Fenofibrate, UV Spectrophotometry.

Introduction and Experimental

Rosuvastatin calcium is chemically bis [(E)-7 [4-(4-fluorophenyl)-6 isopropyl-2-[methyl (methyl-sulphonyl) amino] pyrimidin-5-yl] (3R,5S) -3,5-dihydroxyhept-6-enoic acid] Calcium salt.[1,2] It is a lipid lowering drug. It inhibits the enzyme 3-hydroxry-3-methyl glutaryl coenzyme A (HMG-CoA) reductase, the rate limiting enzyme that converts HMG-CoA to mevalonate;a precursor of cholesterol and thereby checks the synthesis of cholesterol. It is used in the treatment of hypercholesterolemia and dyslipidemia.The typical dose of rosuvastatin calcium is 5-40 mg per day and it reduces 40-70% LDL level[3]. A survey of literature showed few UV spectrophotometric[4-9], few HPLC[10-14], few HPTLC[15-16] two chromatography stability indicating method[17], few LC-MS method[18-20] and few solid phase extraction using tandem mass spectroscopy methods[21] are available for the estimation of rosuvastatin in pharmaceutical preparation and in biological fluids.
Fenofibrate is a drug of the fibrate class[22]. Fenofibrate is chemically propan-2-yl 2{4-[(4-chlorophenyl)-carbonyl] phenoxy}-2-methylpropanoate.It is mainly used to reduce cholesterol levels in patients at risk of cardiovascular disease[23]. Like other fibrates,it reduces both low density lipoprotein(LDL) and very low density lipoprotein(VLDL) levels, as well as reducing triglycerides(TG) level. It also increases high density lipoprotein (HDL) levels[24-25]. It is used alone or in combination with statins in the treatment of hypercholesterolemia and hypertriglyceridemia[26]. A survey of literature showed few UV spectrophotometric[27-29],few HPLC[30-33],one UPLC method[34] and few HPTLC[35-36] methods are available for estimation of fenofibrate in pharmaceutical preparation and in biological fluids.

Apparatus:
A UV – Visible double beam spectrophotometer (JASCO), model no. V-530 with 1 cm matched quartz cells was used for experiments. A Sartorius analytical balance was used.

Chemicals and Reagents:
Methanol [AR Grade] was used in the present study. Methanol [AR Grade] was procured from Finar Chemicals Ltd.Ahmedabad,India. Pure rosuvastatin calcium obtained from cipla Ltd Patalganga, Raigadh and pure Fenofibrate obtained from Smurthi Ltd. Solapur as a gift sample. Tablet of rosuvastatin and fenofibrate were purchased from local market for analysis.

Preparation of Standard Stock Solution:
An accurately weighed quantity of about 10 mg of rosuvastatin calcium was taken in 100 ml volumetric flask dissolved in sufficient quantity of methanol then sonicated for 15 min and diluted to 100 ml with the same solvent so as to get the concentration of 100 µg/ml.s An accurately weighed quantity of about 10 mg of fenofibrate was taken in 100 ml volumetric flask dissolved in sufficient quantity of methanol then sonicated for 15 min and diluted up to 100 ml with the same solvent so as to get the concentration of 100 µg/ml. This stock solution is used for making dilutions for calibration curve.

Determination of λ Max:
The standard solution of rosuvastatin calcium and fenofibrate were separately scanned at different concentration in the range of 200-400 nm and the λ max was determined. The overlain spectrum of both the drugs is also run.

Preparation of Calibration Curve:
For each drug appropriate aliquots were pipette out from standard stock solution into the series of 10 ml volumetric flask and the volume was made up to the mark with methanol to get concentration of 1-10 µg/ml of rosuvastatin calcium and 2-20 µg/ml of fenofibrate. Solutions of different concentrations for each drug were analysed at their respective wavelengths and absorbances were recorded.

Preparation of Mixed Standard Solution:
Accurately 10 mg of rosuvastatin calcium and 67 mg fenofibrate were weighed into 100 ml clean and dry volumetric flask and 50 ml of methanol was added. This mixed standard solution was sonicated for 10 minutes and then volume made up to mark with methanol and prepared solution was subjected to UV analysis.

Preparation of Stock Solution of Tablet Formulation:
Ten tablets of Razel-F[10] containing 10 mg of rosuvastatin calcium and 67 mg of fenofibrate were weighed and finely powdered separately. Powder equivalent to 10 mg of rosuvastatin calcium and 67 mg of fenofibrate was weighed and transferred to a sintered glass crucible and drug was extracted with three 20 ml quantities of methanol, and then final volume of the solution was made up to 100 ml with methanol to get a stock solution containing 100 µg/ml of rosuvastatin calcium and 670 µg/ml fenofibrate, and further dilutions were made to get a concentration of 1µgm/ml of rosuvastatin calcium and6.7 µg/ml of fenofibrate. The contents were mixed thoroughly and filtered through a 0.45 µ membrane filter.

Recovery:
To evaluate the accuracy, precision and reproducibility of the method, known amount of pure drug was added to the analyzed sample of tablet powder and the mixture was analyzed for the drug content using the proposed method. The percentage recovery was found to be within range. The recovery experiments indicated the absence of interference from the commonly encountered Pharmaceutical additives and excipients.

Table-1: Result of UV analysis

Parameters	Rosuvastatin	Fenofibrate
Detection Wavelength	244nm	286.7nm
Beer's Law Limit	1-10µg/ml	2-20µg/ml
Molar Absorptivity	4.3×10^4 L/mol.cm	1.7×10^4 L/mol.cm
Regression Equation	y = mx + c	y = mx + c
Slope	0.046	0.049
Intercept	-0.016	0.002
Correlation Coefficient	0.998	0.999

Table-2: Result of analysis of tablet formulation

Formulation	Drug	Label Claim (mg)	%Label Claim*, Mean ± S.D.	% R.S.D.
Tablet	Rosuvastatin	10mg	99.87±0.000516	0.000517
	Fenofibrate	67mg	98.51±0.00103	0.00104

S.D. - Standard Deviation, R.S.D. - Relative Standard Deviation, *Average of six determinations.

Table-3: Result of recovery study

Formulation	Drug	Label Claim (mg)	%Recovery Estimated*, Mean ± S.D.	% R.S.D.
Tablet	Rosuvastatin	10mg	100.33±0.000577	0.000575
	Fenofibrate	67mg	99.10±0.000577	0.000582

S.D. - Standard Deviation, R.S.D. - Relative Standard Deviation, *Average of six determinations.

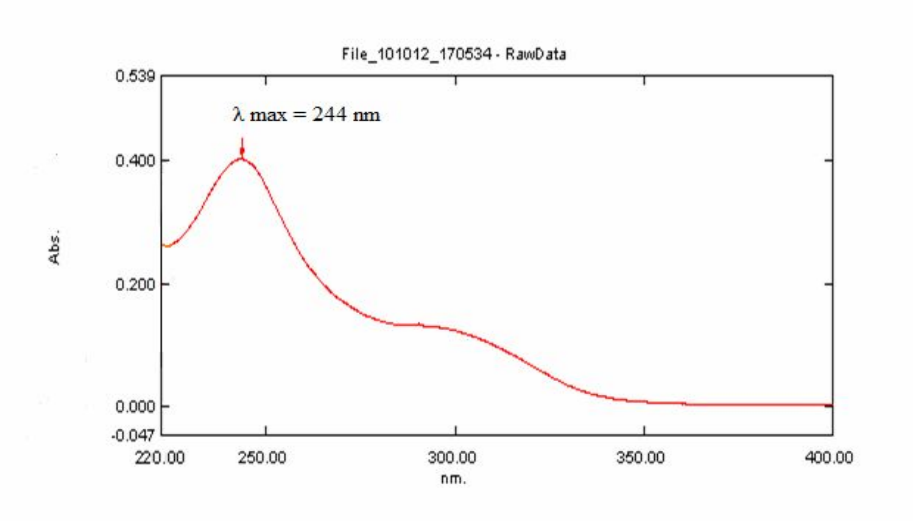

Figure 1: λ_{max} for Rosuvastatin calcium

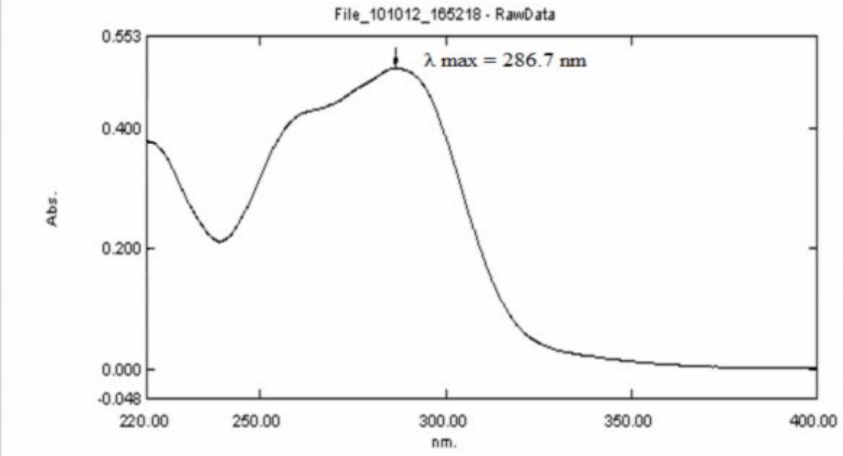

Figure 2: λmax for fenofibrate

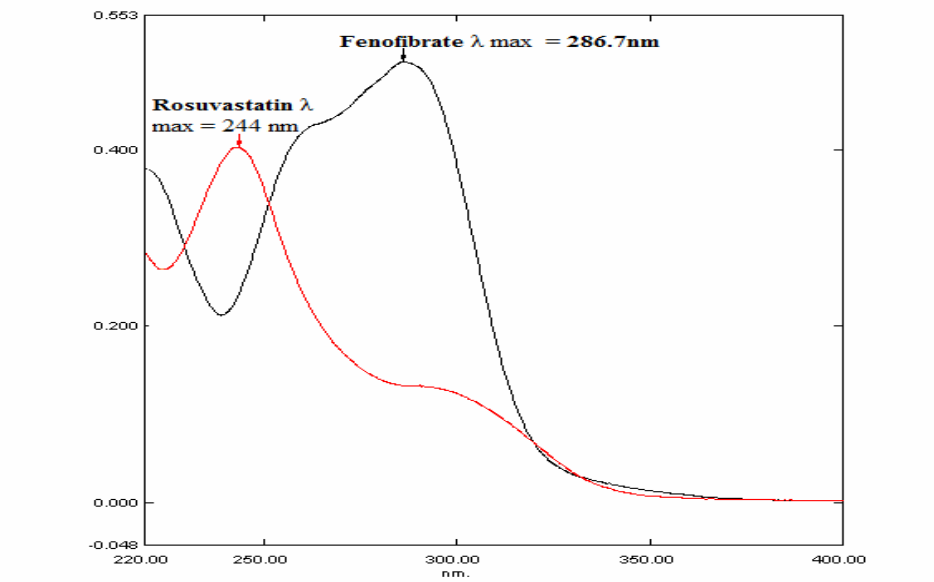

Figure 3: UV overlain spectra for Rosuvastatin and Fenofibrate

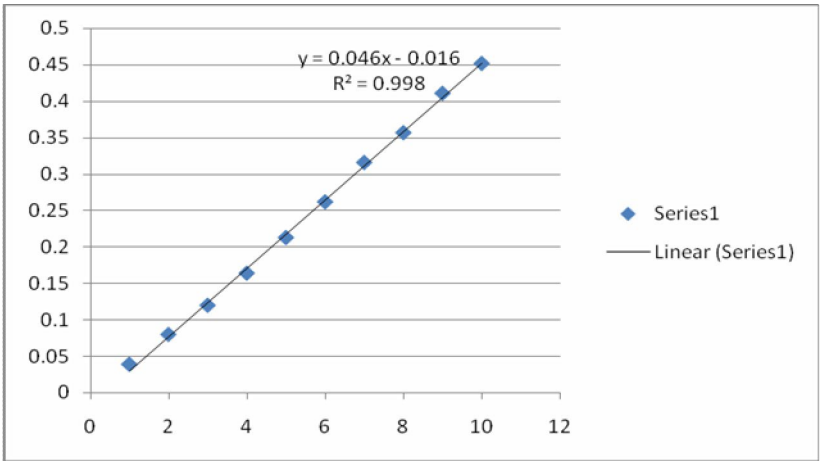

Figure 4: Calibration curve for rosuvastatin calcium

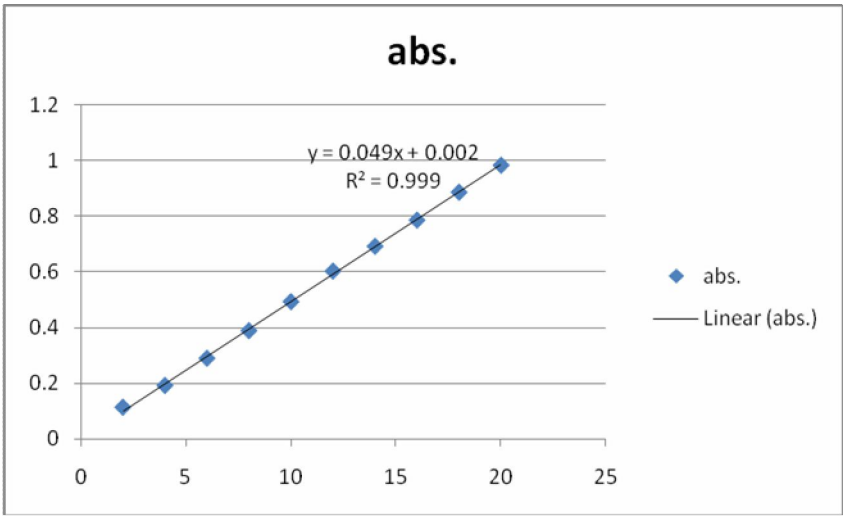

Figure 5: Calibration curve for fenofibrate

Results and Discussion

The proposed method for determination of rosuvastatin calcium and fenofibrate showed molar absorptivity 4.3×10^4L/mol.cm and 1.7×10^4L/mol.cm .The result of UV analysis has been shown in Table-1 indicates that the representative calibration curve of rosuvastatin calcium and fenofibrate were plotted at 244nm and 286.7nm respectively. A linear relationship was obtained for both the drugs in the concentration range of 1-10µg/ml for rosuvastatin calcium and 2-20µg/ml for fenofibrate. Linear regression of absorbance on concentration gave the equation,

For, Rosuvastatin calcium
$y = 0.046x – 0.016$
Correlation coefficient (R^2) = 0.998
For, Fenofibrate
$y =0.049x + 0.002$
Correlation coefficient (R^2) = 0.999

The result of UV analysis for tablet formulation has been shown in Table-2 indicate that none of the pharmaceutical excipients interfered in the estimation of rosuvastatin calcium and fenofibrate in the UV spectrophotometric method. The calculation of concentration for tablet formulation done by simultaneous equation method. The result of recovery study shown in Table-3 clearly indicate that the percentage recovery was found to be within range for both the drugs in the range of 99.50% to 101% for rosuvastatin calcium and 98.95% to 99.40% for fenofibrate.

Conclusion:

The Spectrophotometry provides versatile techniques for analyse drug in multicomponent pharmaceutical formulation in presence of various interferences. The present work describes simple, economical and non interfering spectrophotometric method for the estimation of rosuvastatin calcium and fenofibrate using simultaneous equation method. The method was found to be economic, simple, precise, accurate and reproducible during analysis of drug formulations containing the two drugs.

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