



**DETERMINATION AND ESTIMATION OF CONCENTRATION OF ROSUVASTATIN
CALCIUM AND EZETIMIBE TABLET IP IN A BULK DRUG AND PHARMACEUTICAL
FORMULATION BY UV- VISIBLE SPECTROPHOTOMETRIC USING
SIMULTANEOUS EQUATION METHOD**

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ABSTRACT

This article focuses on the UV Spectrophotometric estimation of a drug combination i.e Rosuvastatin Calcium and Ezetimibe, which is used in the treatment of hypercholesterolemia and hyperlipidemia. Rosuvastatin Calcium is a HMG-CoA inhibitor while Ezetimibe is an intestinal cholesterol inhibitor. The drug obeyed the Beer's law and showed good correlation. Acetonitrile was used as a solvent. A simple, economic and precise Spectrophotometric method was developed for simultaneous estimation of Rosuvastatin Calcium and Ezetimibe in a combined dosage form.

KEYWORDS: Rosuvastatin Calcium, Ezetimibe, UV-spectroscopy, Method development, λ_{max} .

INTRODUCTION

Rosuvastatin calcium: It is a 3-hydroxy-3-methyl glutaryl (HMG)-CoA reductase inhibitor. It works by slowing production of cholesterol in a body to decrease the amount of cholesterol that build up on the walls of arteries and blocks the blood flow to heart, brain.

It inhibits the enzyme 3-hydroxy-3-methyl glutaryl coenzyme A, the rate limiting enzyme that converts HMG-CoA to mevalonate; a precursor of cholesterol.

Empirical formula: $C_{44}H_{54}CaF_2N_6O_{12}S_2$

Molecular weight: 1001.14

Color: White to off-white.

Solubility: Soluble in organic solvents.

IUPAC name: calcium;(E,3R,5S)-7-[4-(4-fluorophenyl)-2-[methyl(methylsulfonyl)amono]-6-propan-2-yl]pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoate.

Ezetimibe: It is a non- statin lipid lowering medication. It is an azetidinone derivative which inhibits the absorption of cholesterol in a intestine by blocking Niemann-Pick C1 like protein.

Empirical formula: $C_{24}H_{21}F_2NO_3$

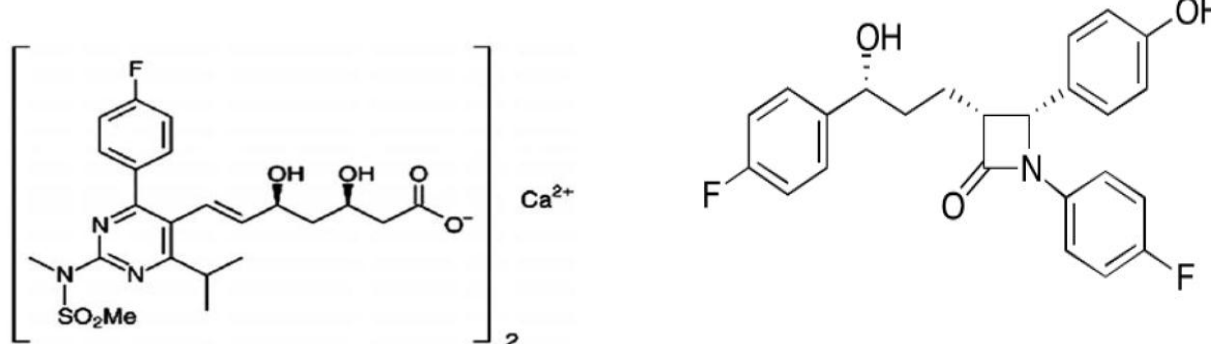
Molecular weight: 409.4

Color: White solid

Solubility: Soluble in Acetonitrile, ethanol and Methanol

Chemical Structure:

Chemical structure:



IUPAC name: (3S, 4S)-1-fluorophenyl)-3-[(3S)-3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)azetidin-2-one

Instrumentation

A UV- Visible double beam spectrophotometer (SHIMADZU), model no.UV-1900i, Digital analytical balance and ultra sonicator were used.

Chemicals and Reagents

Acetonitrile: [AR Grade]

Rosukem 10 tablet manufactured by Alkem health science

Ezedoc 10 tablet manufactured by Lupin ltd.

Roseday -EZ10 tablets manufactured by Windlas Biotech Pvt. Ltd. purchased from local pharmacy was used for analysis.

Method:

Selection of Solvent and Wavelength:

The UV spectra of Rosuvastatin Calcium and Ezetimibe differ in solvent like Acetonitrile was recorded; both the drugs showed good absorbance when dissolved in Acetonitrile. Hence, Acetonitrile was selected as the solvent for the method.

The two drugs showing good absorbance at wavelength of 244nm and 247nm, hence selected as λ_{max} of Rosuvastatin Calcium and Ezetimibe respectively.

Preparation of standard stock solution:

Standard stock solution of Rosuvastatin Calcium and Ezetimibe were prepared by dissolving 10 mg to each drug in a 100 ml volumetric flask with sufficient amount of solvent Acetonitrile then sonicated it for 10 min and diluted up to 100 ml with the same solvent to get concentration of $100\mu\text{g/ml}$ i.e 100ppm.

Preparation of working standard solutions:

1ml of above stock solution was taken and diluted upto 10 ml with the Acetonitrile to get solution of concentration $10\mu\text{g/ml}$ i.e 10 ppm. Similarly solutions of concentration 20ppm, 30ppm, 40ppm and 50ppm were prepared.

Preparation of stock solution for a combined drug:

Two Roseday-EZ10 tablets each containing 10 mg of Rosuvastatin Calcium Calcium and Ezetimibe were powdered and 10 mg of it was weighed and transferred into the 100 ml volumetric flask.

Sufficient amount of Acetonitrile were added and sonicated for 10 min to affect the complete dissolution of the drugs and then diluted upto 100 ml with the same solvent to get the concentration of $100\mu\text{g/ml}$ i.e 100ppm.

The solution of concentration 10 ppm to 50 ppm were prepared from the standard stock solution of a combined drug.

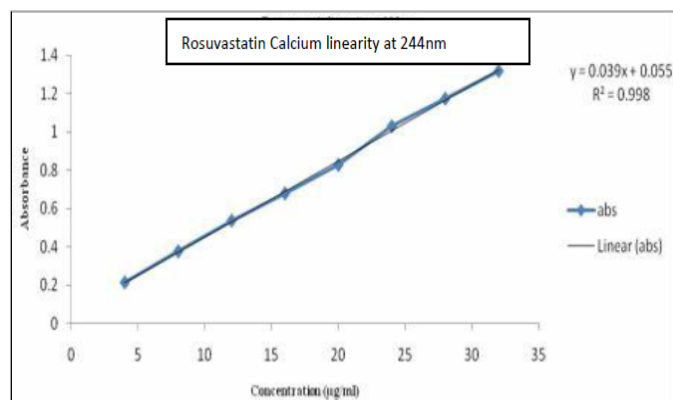


Figure 1: Calibration graph of rosuvastatin calcium at 244nm.

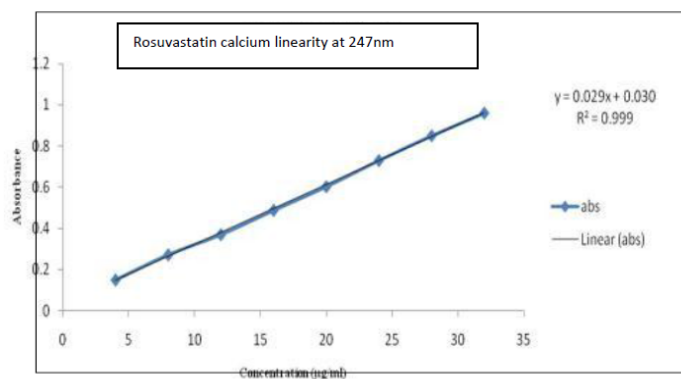


Figure 2: Calibration graph of rosuvastatin calcium at 247nm.

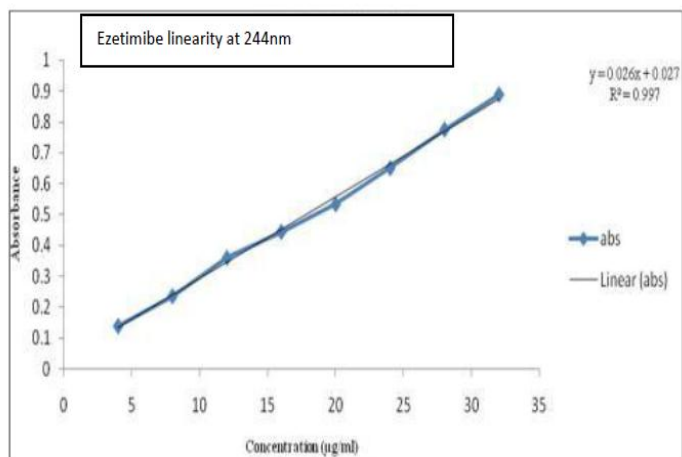


Figure 3: Calibration graph of ezetimibe at 244nm.

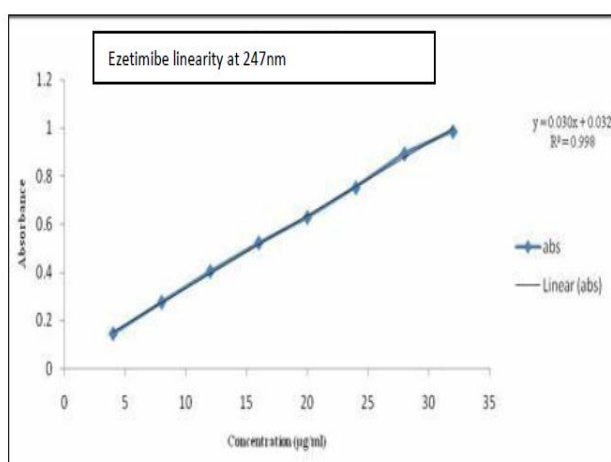


Figure 4: Calibration graph of ezetimibe at 247nm.

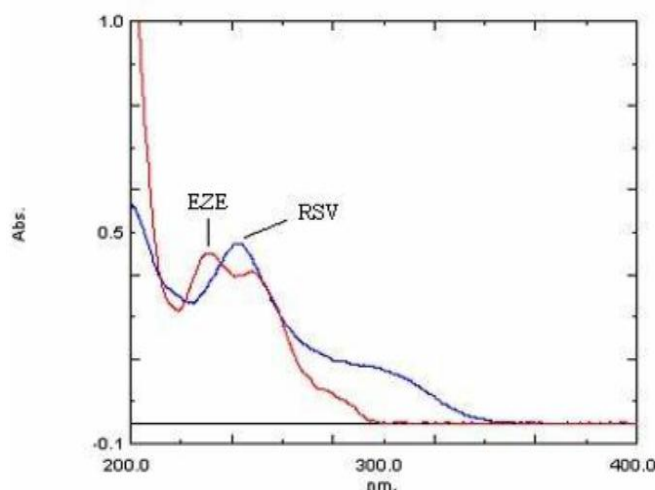


Figure 5: Overlain spectrum of 10µg/ml of Rosuvastatin Calcium and Ezetimibe.

Table 1: Result of UV analysis.

Parameters	Rosuvastatin calcium	Ezetimibe
Detection wavelength	244nm	247nm
Beer's law limit	10-50µg/ml	10-50µg/ml
Regression equation	y=mx+c	y=mx+c
Slope	0.0348	0.0485

Intercept	0.0074	0.04995
Correlation Coefficient	0.9995	0.99977

Table 2: Result of recovery Study.

Formulation	Drug	Label claim (mg)	%Recovery Estimated, Mean \pm S.D	%R.S.D
Tablet	Rosuvastatin Calcium	10	100.33 \pm 0.000577	0.000575
	Ezetimibe	10	99.10 \pm 0.000577	0.000583

Table 3: Absorbance values of rosuvastatin calcium with acetonitrile.

Sr.no	Concentration (μ g/ml)	Absorbance at 244nm	Absorbance at 247nm
1	10	-0.001	0.001
2	20	0.062	0.076
3	30	0.161	0.150
4	40	0.215	0.217
5	50	0.302	0.302

Table 4: Absorbance values of Rosuvastatin Calcium + Ezetimibe with Acetonitrile.

Sr.no	Concentration (μ g/ml)	Absorbance at 244nm	Absorbance at 247nm
1	10	0.102	-0.000
2	20	0.178	-0.076
3	30	0.261	0.167
4	40	0.318	0.237
5	50	0.405	0.319

RESULT AND DISCUSSION

Rosuvastatin Calcium exhibits the absorption maxima at 244nm and Ezetimibe at 247nm. A linear relationship was obtained for both the drugs in the concentration range of 10 to 50 μ g/ml i.e. 10ppm to 50 ppm. A linear relationship was obtained for both the drugs in a concentration range of 10-50 μ g/ml. Linear regression of absorbance on concentration gave the equation,

For, Rosuvastatin Calcium $y=0.039x+0.056$ and correlation coefficient=0.9995

For, Ezetimibe $y=0.030x+0.031$ and correlation coefficient =0.9997

The calculation of concentration for tablet formulation done by simultaneous equation method.

CONCLUSION

The obtained values suggest that the proposed UV – Spectrophotometric method provides simple, precise, accurate and quantitative analytical method for determination of Rosuvastatin Calcium and Ezetimibe by simultaneous equation method. The linearity in the graph indicates that the Beer's Lambert law was obeyed. The spectrophotometry provides versatile techniques for analyze drug.

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