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Research Article

Development and validation of UV spectrophotometric method for simultaneous estimation of propranolol hydrochloride and rosuvastatin calcium in bulk drug and pharmaceutical dosage form

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Absorbance ratio (Q- point) method

Abstract

A new, simple and sensitive UV spectrophotometric method has been developed for simultaneous quantitative determination of propranolol hydrochloride and rosuvastatin calcium in bulk and pharmaceutical dosage form. This is achieved by simultaneous equation (Vierodt's method) and absorbance ratio (Q- point) method. Propranolol hydrochloride and rosuvastatin calcium exhibits maximum absorbance at 289 nm and 243 nm respectively in methanol as solvent. Beer's law was found to be obeyed in the concentration range 2-40 µg/ml for propranolol hydrochloride and 2-42 µg/ml or rosuvastatin calcium. Method were validated for linearity, accuracy, precision, LOD, LOQ as per ICH guidelines.

1. Introduction

In spectrophotometric analysis a source of radiation is used that extend into the ultraviolet region of the spectrum. The kind and amount of radiation absorbed by a molecule depend upon the structure of the molecule, the amount of radiation absorbed also depend upon the number of molecules interacting with the radiation. The study of these dependencies is called absorption spectroscopy.

The multicomponent formulations have gained a lot of importance now a day due to greater patient acceptability, increased potency and decreased side effects. The quantitative analysis of such multicomponent formulations is very important. One of the quantitative procedures for multicomponent formulations is the simultaneous spectrophotometric method, which utilizes the measurement of intensity of electromagnetic radiation emitted or absorbed by the analyte.

Vierodt's method:

If the sample contain two absorbing drugs each of which absorb at λmax of the other, it may be possible to determine both drugs by Vierodt's method. Simultaneous estimation of two drugs can be possible only when λmax of both drug components are reasonably dissimilar and two components do not interact chemically. It is calculated by formula,

$$Cpro = \frac{A_2 ay_1 - A_1 ay_2}{ax_2 ay_1 - ax_1 ay_2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$Cros = \frac{A_1 ax_2 - A_2 ax_1}{ax_2 ay_1 - ax_1 ay_2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

Whereas,

ax_1 and ax_2 are absorptivities of PRO at λ_1 and λ_2 respectively.
ay_1 and ay_2 are absorptivities of ROS at λ_1 and λ_2 respectively.
A_1 an A_2 are absorbance of sample at λ_1 and λ_2 respectively.

Absorbance ratio method

It is modification of simultaneous equation method. It is based on the principle that for the substance which obeys

Beer's law at all wavelength, the ratio of absorbances at any two wavelengths is a constant value independent of concentration or pathlength. It is also called as isoabsorptive point method or Q method.

In absorbance ratio method, absorbances are measured at two wavelengths one being the λmax of one of the component and other being wavelength of equal absorptivity of the two components. It is calculated by formula given below,

$$C_{PRO} = \frac{Qm-Qy}{Qx-Qy} \times \frac{A}{ax_1} \ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

$$C_{ROS} = \frac{Qm-Qx}{Qy-Qx} \times \frac{A}{ax_2} \ldots\ldots\ldots\ldots\ldots\ldots\ldots (4)$$

Whereas,

C_{PRO}- Concentration of propranolol hydrochloride

C_{ROS}- Concentration of rosuvastatin calcium

A-Absorbance of sample at isoabsorptive wavelength

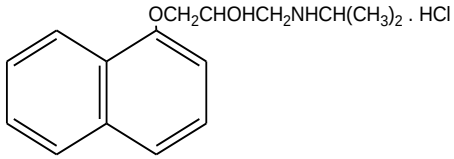
Ax_1 and Ax_2- Absorptivity of PRO and ROS at isoabsorptive point respectively.

$$Q_m = \frac{Absorbance\,of\,sample\,at\ \lambda\text{max}\ of\,one\,of\,the\,component(\lambda_2)}{Absobance\,of\,sample\,at\,isoabsorptive\,wavelengt\,h}$$

$$Q_{PRO} = \frac{Absorptivity\,of\,PRO\,at\ \lambda\text{max}\ of\,one\,of\,the\,component(\lambda_2)}{Absorptivity\,of\,PRO\,at\,isoabsorptive\,wavelengt\,h}$$

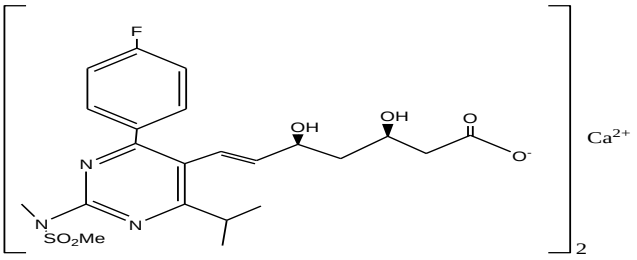
$$Q_{ROS} = \frac{Absorptivity\,of\,ROS\,at\ \lambda\text{max}\ of\,one\,of\,the\,component(\lambda_2)}{Absorptivity\,of\,ROS\,at\,isoabsorptive\,wavelengt\,h}$$

Propranolol hydrochloride is non-selective beta-adrenergic receptor blocking agent. Propranolol hydrochloride competitively blocks beta-adrenergic receptor and gives membrane-stabilizing action. It is stable, white crystalline solid readily soluble in water and ethanol and methanol.



2-Propranol,1-[(1-methylethyl)amino]-3-(1-napthalenyloxy)-hydrochloride

Rosuvastatin calcium is a synthetic lipid-lowering agent. Rosuvastatin is aninhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzymecatalyzes the conversion of HMG-CoA to mevalonate, an early and rate-limiting step incholesterol biosynthesis. Rosuvastatin calcium is a white amorphous powder that is sparingly soluble in water and methanol, and slightly soluble in ethanol. Rosuvastatin is a hydrophilic compound with a partition coefficient (octanol/water) of 0.13 at pH of 7.0.



Bis[(E)-7-[4-(flurophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino] pyrimidin-5-yl]-(3R,5S)-3-5-dihydroxyhept-6-enoic acid] calcium salt

At present no any UV spectrophotometric method was reported in literature for quantitative estimation of propranolol hydrochloride and rosuvastatin calcium. Hence, attempt was made to develop simple, precise and accurate UV spectrophotometric method for simultaneous estimation of both the drugs by simultaneous equation (Vierodt's method) and absorbance ratio (Q- point) method. Further, method were validated for accuracy, precision, LOD, LOQ as per ICH guidelines.

2. Material and method

Propranolol hydrochloride and rosuvastatin calcium was obtained as a gift sample from Watson pharma, Mumbai and Okasa pharma, Satara (MH) respectively. Methanol of analytical reagent was selected as common solvent for method development. UV visible spectrophotometer (Shimadzu, Japan) with 1 cm quartz cells was used in present investigation for absorbance measurement.

2.1 Calibration curve of propranolol hydrochloride and rosuvastatin calcium:

100 mg of propranolol hydrochloride and rosuvastatin calcium was dissolved separately in 100 ml volumetric flask containing methanol as solvent to form stock solution having strength 1000 µg/ml. From that, 10 ml of solution was withdrawn and diluted upto 100 ml to give stock solution having strength 100 µg/ml and using this stock solution various concentrations were prepared in the range 2-40 µg/ml. firstly λmax of both the drug was determined using concentration 10 µg/ml. Then absorbances of both the drugs were determined using UV spectrophotometer at the irrespective λ max.

2.2 Determination of isoabsorptive point for propranolol hydrochloride and rosuvastatin calcium:

For simultaneous estimation of propranolol hydrochloride and rosuvastatin calcium in pure and pharmaceutical dosage form by absorbance ratio method it was necessary to determine isoabsorptive point in which both drugs showed absorption at particular wavelength. It can be determined spectrophotometrically by preparing various concentrations in beers range of both pure drugs and obtaining overlay spectra.

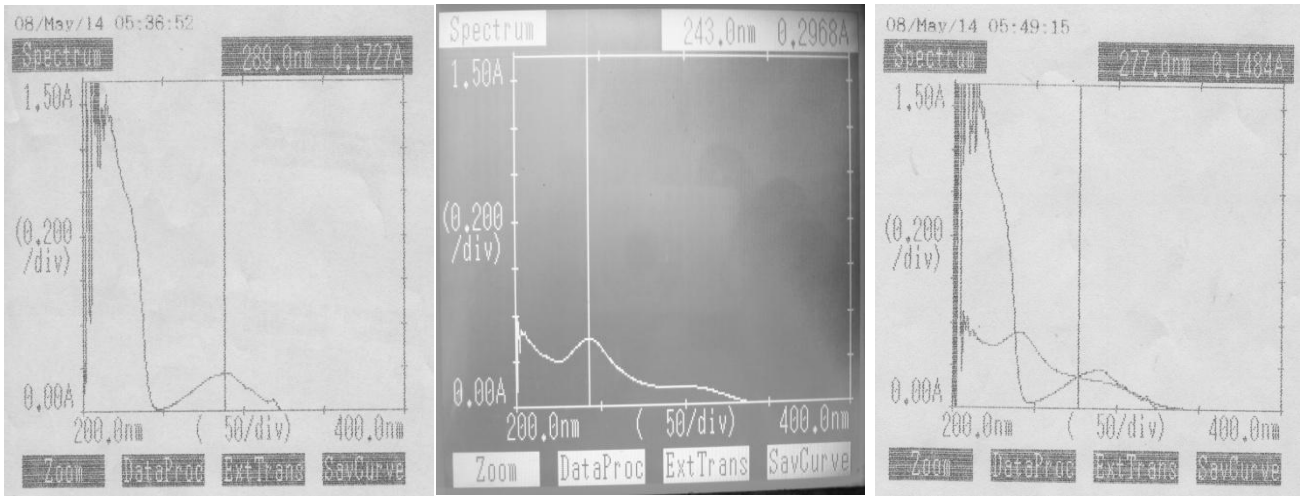
2.3 Procedure for estimation of drug in pharmaceutical dosage form:

Rectangular (2*3 cm) gastroretentive bilayer floating film containing 5 mg of rosuvastatin calcium and 40 mg of propranolol hydrochloride was dissolved in 100 ml volumetric flask containing methanol as solvent with stirring and kept aside for 6-8 hours. Further dilutions were prepared so that concentration of the sample solution will be in the Beers range of respective drugs.

3. Result and discussion

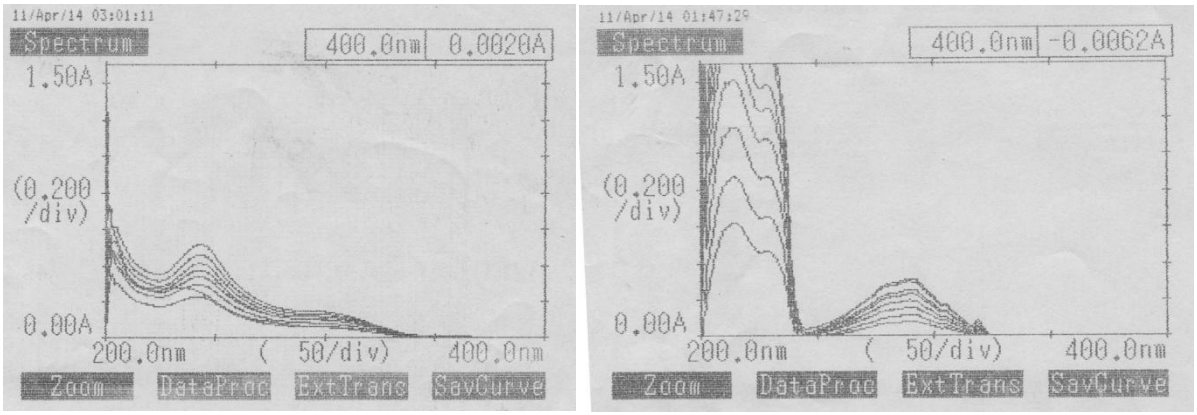
Propranolol hydrochloride and rosuvastatin calcium showed λmax at 289 nm and 243 nm respectively. Linearity was found in the range 2-42 µg/ml with correlation coefficient (r) 0.9984 for propranolol hydrochloride and 2-40 µg/ml with correlation coefficient (r) 0.9996 for rosuvastatin calcium. Absorptivity values are calculated by preparing multiple dilutions of 10 µg/ml solution of both pure drug and taking average mean of the same. To evaluate the validity and reproducibility of the method known amount of pure drug was added to the analysed sample of film and mixture was analysed for the drug content using proposed method. The recovery experiments indicated the absence of interference from the commonly encountered pharmaceutical additive and excipients.

Figure 1: λmax of a) propranolol hydrochloride (289 nm), b) rosuvastatin calcium (243 nm) and c) isoabsorptive point (277 nm)



a b c

Figure 2: overlay spectra of a) propranolol hydrochloride (289nm) and b) rosuvastatin calcium (243nm)



a b

Table 1: Calibration curve of propranolol hydrochloride and rosuvastatin calcium

Propranolol hydrochloride (289nm)			Rosuvastatin calcium (243nm)		
Concentration (µg/ml)	**Absorbance (Mean±SD)**	**SE (n=3)**	**Concentration (µg/ml)**	**Absorbance (Mean±SD)**	**SE (n=3)**
10	0.1484±0.002	0.0011	12	0.4117±0.0002	0.0001
12	0.1734±0.004	0.0026	16	0.5678±0.0002	0.0001
14	0.2686±0.000	0.0004	20	0.7331±0.0003	0.0001
16	0.2899±0.003	0.0017	24	0.9052±0.0003	0.0001
018	0.3244±0.006	0.0039	28	1.0540±0.0032	0.0018
20	0.3495±0.008	0.0050	32	1.2000±0.0100	0.0057

Regression equation	Y= Mx+C	Regression equation	Y= Mx+C
Beers law limit	2-42 µg/ml	Beers law limit	2-40 µg/ml
Slope	0.03857	Slope	0.039801
Intercept	-0.03892	Intercept	-0.06366
Correlation	0.99840	Correlation	0.99962
Sandell's sensitivity	0.043744	Sandell's sensitivity	0.026427

Table 2: Absorptivity values for propranolol hydrochloride and rosuvastatin calcium at respective λmax and isoabsorptive point

	Absorptivity of propranolol hydrochloride			Absorptivity of rosuvastatin calcium		
	289 nm	**243 nm**	**277 nm**	**243 nm**	**277 nm**	**289 nm**
Mean (n=3)	228.6	298.8	146.3	378.3	141.1	103.0
± SD	1.000	0.5859	1.237	1.336	1.311	1.261
SE	0.5774	0.3383	0.7113	0.7713	0.7572	0.7278

Table 3: Analysis of bilayer film formulation

Film component	Labelled claim (mg)	Amount found (mg)	% purity± SD	SE (n=3)
Propranolol hydrochloride	40	39.492	98.73±0.05937	0.03428
Rosuvastatin calcium	05	4.877	97.54±0.05508	0.03180

Table 4: Statistical evaluation of precision

Drug	Film strength	Interday precision			Intraday precision		
		Mean	**± SD**	**SE**	**Mean**	**± SD**	**SE (n=3)**
Propranolol hydrochloride	40 mg	39.16	0.4359	0.2517	0.3972	0.07638	0.04410
	20 mg	19.50	0.2574	0.1486	19.35	0.04635	0.02674
Rosuvastatin calcium	05 mg	4.77	0.1000	0.05773	4.877	0.06807	0.03930
	10 mg	9.723	0.1343	0.07753	9.870	0.05000	0.02887

Table 5: data of validation parameters

Parameters	Observed values	
	Propranolol hydrochloride	Rosuvastatin calcium
Linearity (r)	0.99840	0.99962
Accuracy (% recovery)	98.73	97.54
LOD (µg/ml)	0.3279	0.1961
LOQ (µg/ml)	0.9937	0.5944

4. Conclusion

Simultaneous equation (Vierodt's method) and absorbance ratio method were found to be simple, precise and accurate. Statistical analysis of the results has been carried out revealing high accuracy and good precision. The developed methods can be used in routine analysis of propranolol hydrochloride and rosuvastatin calcium in bulk and combined pharmaceutical dosage forms.

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