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DEVELOPMENT AND VALIDATION OF Q- ABSORBANCE RATIO SPECTROPHOTOMETRIC METHOD SIMULTANEOUS ESTIMATION OF SIMVASTATIN AND LABETALOL HCL IN COMBINED DOSAGE FROM

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ABSTRACT

A simple, precise, accurate and economical methods without any extraction step' The solvent used was 0.25N sodium hydroxide. Two wavelengths 246.00nm (λ max of Labetalol HCl) and 243.48nm (Isoabsorptive point) were selected for estimation of Labetalol HCl and Simvastatin for Q-absorbance ratio method. The concentrations of a drugs were determined by a using ratio of Q absorbances at isoabsorptive points and at the λ-max of Labetalol HCl methods was a successfully applied to pharmaceuticals dosage froms.

KEYWORD: Labetalol HCl, Simvastatin, 0.25N sodium hydroxide.

INTRODUCTION

Simavastatin is 2,2-Dimethylbutanoicacid(1S,3R,7S,8S,8aR)-1,2,3,7,8,8ahexahydro- 3,7-dimethyl-8-[2-[(2R,4R)- tetrahydro-4-hydroxy-6 oxo2H pyran-2yl]ethyl]1-napthalenyl ester Simvastatin belongs to a class of drugs called HMG-CoA reductase inhibitors commonly called statins that derived synthetically from fermentation products of Aspergillus terreus. All statins act by inhibiting 3-hydroxy-3- methylglutarylcoenzyme (HMG-CoA). A HMG-CoA reductase.[1,2] The rate limiting enzyme of the HMG-CoA reductase pathway, the metabolic pathway responsible for the endogenous production of cholesterol mainly used for the treatment of dyslipidemia and the prevention of cardiovascular diseases. Simvastatin is prodrug which is converted into its β- hydroxy which inhibits.[3] HMG CoA reductase (3-hydroxy-3-methyl glutaryl Coenzyme A) enzyme, responsible for catalysing the conversion

of HMG CoA to mevalonate a rate limiting step in the synthesis of cholesterol in liver.[4] Labetalol HCl is a selective α1 and non-selective β adrenergic blocker used to treat a high blood pressure. Chemically it is 2-hydroxy-5-{[1-hydroxy-2-(4 phenyl butane-2-lyl) amino] ethyl}benzamide. It has a molecular formula f C19H24N2O3.Hcl and a molecular weight of 328.40g/mol.[5,6]

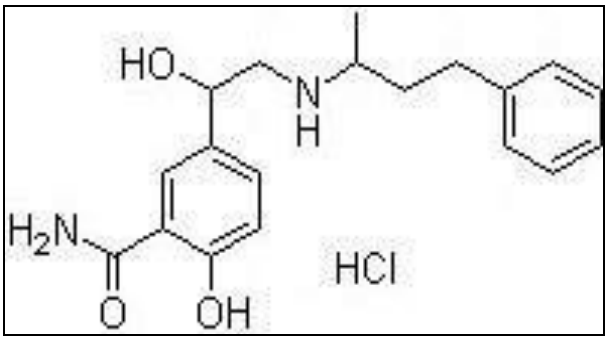

Figure 1: Chemical structure of labetalol HCL.

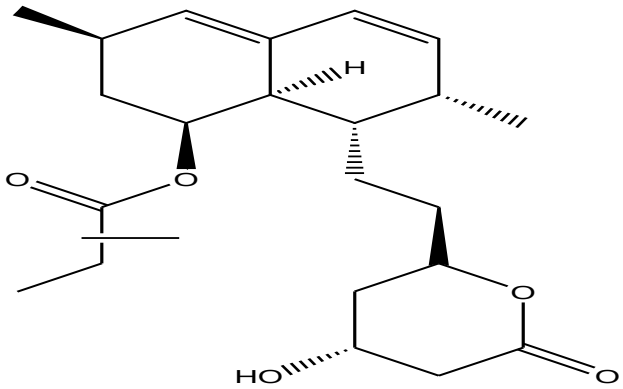

Figure 2: Chemical structure of simvastatin.

Q-Absorbance ratio method

Let it be one drug X and Y

According to Q-Absorbance ratio methods use the ratio of absorbance at two a selected wavelengths. One is a iso-absorptive points and other being the λ-max of one and two components.

Two equations were a constructed as the described below, using the relationship ax1=ay1 at λ1 and L=1. Equations are;

at λ1 $A_1 = {}_{ax1Cx} + {}_{ax1Cy}$ ($ax_1=ay_1$) …. (1)

at λ_2 $A_2 = {}_{ax1Cx} + {}_{ay2Cy}$ ..... (2)

Dividing equation (2) by (1), we get

$A_2/A_1 = (_{ax2Cx} + _{ay2Cy})/(_{ax1Cx} + _{ax1Cy})$ …… (3)

Let Cx/(Cx+Cy)=Fx & Cy/(Cx+Cy)=Fy

Dividing Equation (3) by Cx+Cy, we get

A2/A1 = (ax2Fx+ay2Fy)/(ax1Fx+ax1Fy)

But Fy =1 - Fx

A2/A1 = (ax2Fx+ay2-ay2Fx)/ax1 …… (4)

A2/A1 = (ax2Fx/ax1) – (ay2Fx/ ay1) + (ay2/ay1) (because ax1=ay1)

Let $ax_1 / ax_2 = Qx$, $ay_2/ay_1 = Qy$ & $A_2 / A_1 = QM$

So, QM = FxQx – FyQy + Qy

Fx = (QM-Qy)/(Qx-Qy) …… (5)

This equation it gives a fractions of mixture that a determine the absolute the concentrations of X and Y.

Cx/(Cx=Cy) = (A2/A1)-(ay2/ay1)/(ax2/ax1)-(ay2/ay1) …… (6)

Both equations (5) & (6) gives a fraction, rather than the concentrations of a X and consequently of a Y in the mixture the term of absolutely ratio. As, these are independent of the concentrations only approximate rather than accurate.

If a absolute concentrations of X & Y than rearrange equations (1), we gets.

Cx+Cy = A1/ax1 .. …… (7)

From equation (6) & (7), we get

Cx/(A1/ax1) = (QM-Qy)/(Qx-Qy)

Cx= {(QM-Qy)/(Qx-Qy)}* (A1/ax1) …… (8)

& Cy= {(QM-Qx)/(Qy-Qx)}* (A1/ay1) ……..(9)

Finally equation (8 & 9) gives the absolute concentration value of drug X & Y.[7,8,9]

MATERIAL AND METHOD

A UV Visible double beam spectrophotometer (Shimadzu model UV 1800) attached to computer UV probe 2.33 with spectral width of 2 nm, wavelength accuracy 0.5 nm and pair of 1 cm matched quartz cell was employed. Kindly gifted reference standard of simvastatin and labetalol HCL (Glen mark pharmaceutical) were used for study.

Preparation of standard stock solution

A accurately weighed quantity of about 100mg of simvastatin was a taken in 100ml volumetric flask a dissolved in sufficient quantity of 0.25N NaOH then is a sonicated for a 15min and diluted to 100 ml with the same solvent so as to get the concentrations of a

100µg/ml. An accurate weighed quantity of a about 100mg of labetalol was a taken in 100ml volumetric flask dissolved in sufficient quantity of 0.25N NaOH then sonicated for 15 min and diluted up to 100 ml with the same solvent so as to get the concentration of 100µg/ml.[5]

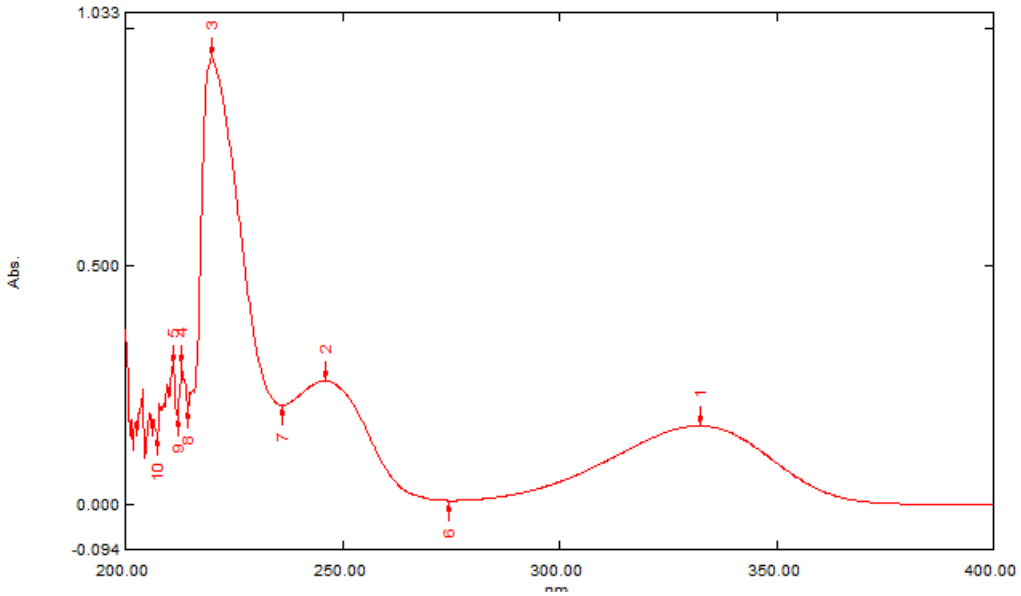

Figure 3: Absorption spectra of labetalol HCL.

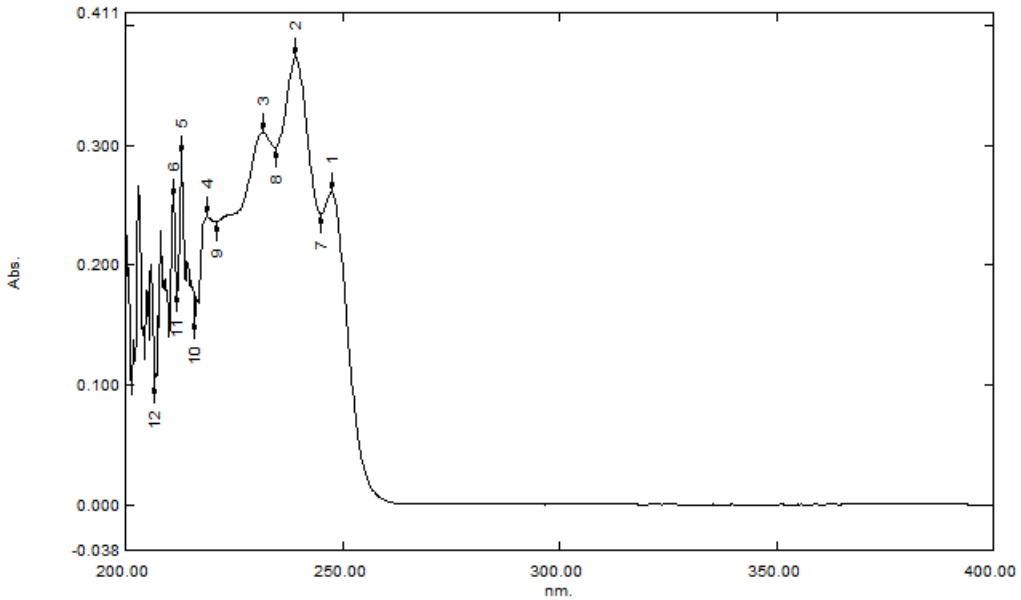

Figure 4: Absorption spectra of simvastatin.

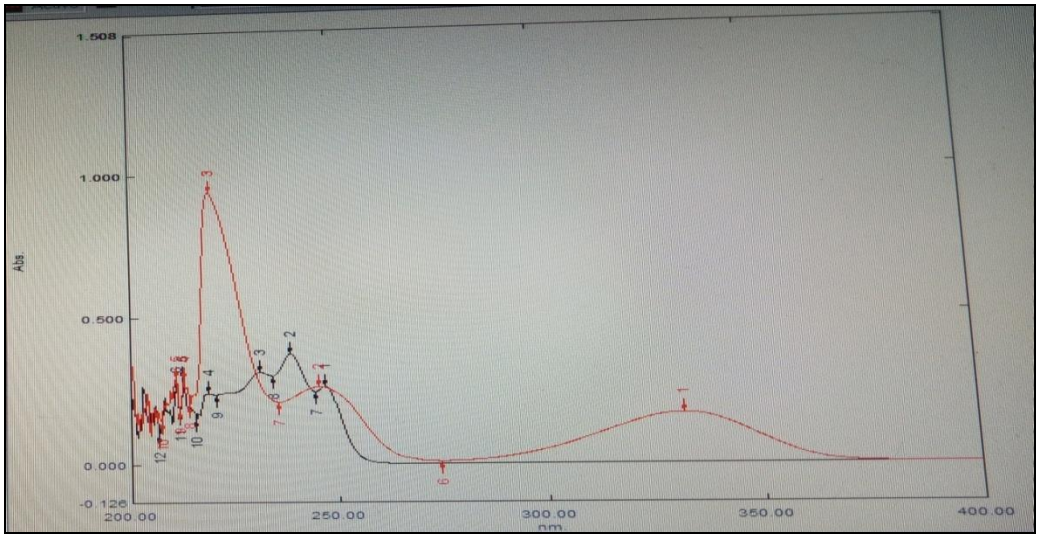

Figure 5: Overlain spectra of Simvastatin and Labetalol HCl.

The maximum absorption (λmax) of Labetalol HCl was found at 246.00 nm and iso-absorptive point at 243.48 nm. Absorption for a series of standard solutions were recorded at selected wavelength.

METHODOLOGY

Q Absorbance ratio method was used ratio of absorbance of two a selected waveleng λ-max. From the overlain spectra of two drugs (as shown in figure 5), it shows that Simvastatin and Labetalol HCl having iso-absorptive point at 243.48 nm. The second wavelength used is 246.00 nm, which is the λmax of Labetalol HCl.[9] Working standard solutions having concentration 2, 4, 6, 8, 10 ppm and 10 µg/ml for Simvastatin and Labetalol HCl were prepared in 0.25N NaOH and the absorbance at 243.48 nm (iso-absorptive point) and 246.00 nm (λmax of Labetalol HCl) were measured.[5]

The concentrations of two drug in the mixture can be calculating by using the equations (8 & 9), we gets,

$Cx = \{(QM-Qy)/(Qx-Qy)\} * (A1/ax1)$

$Cy = \{(QM-Qx)/(Qy-Qx)\} * (A1/ay1)$

where, A1 and A2 are the absorbance of mixture at 243.48 nm and 246.00 nm; ax1 and ay1 are absorptivities of Simvastatin and Labetalol HCl at 243.48 nm; ax2 and ay2 are absorptivities of Simvastatin and Labetalol HCl at 246.00 nm; QM = A2/A1, Qx= ax2/ ax1, Qy = ay2/ay1.[8,9]

Validation of proposed method

Linearity

Linearity was evaluated by preparing different concentration in the range of 2-10 µg/ml for both the drugs and absorption was measured. Each measurement was carried out in triplicate.

Table no. 1: Calibration curve of simvastatin.

Conc. µg/ml	Absorbance
2	0.049
4	0.065
6	0.084
8	0.111
10	0.133

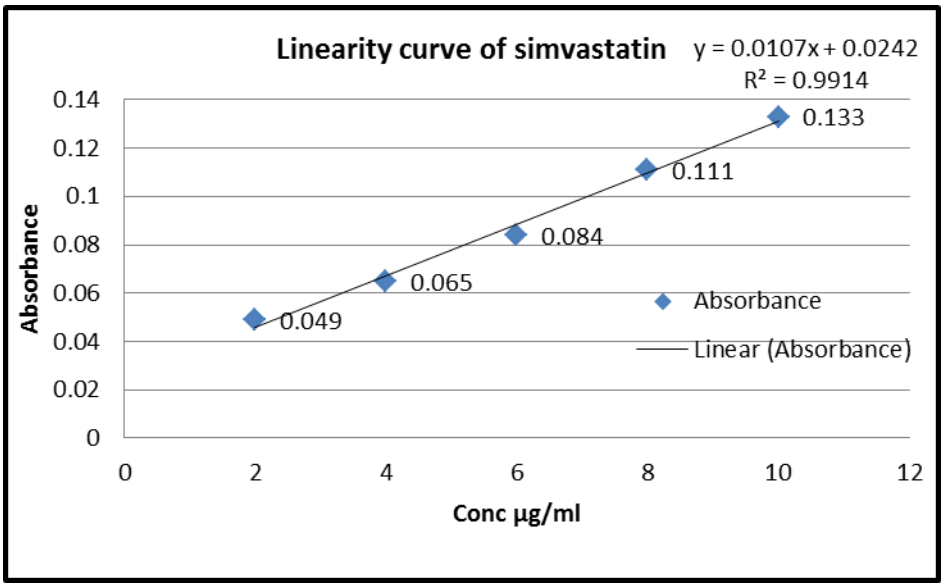

Figure 6: Linearity curve for simvastatin HCL at 246.00nm.

Table no. 2: Calibration curve of labetalol.

Conc. µg/ml	Absorbance
2	0.122
4	0.132
6	0.139
8	0.149
10	0.161

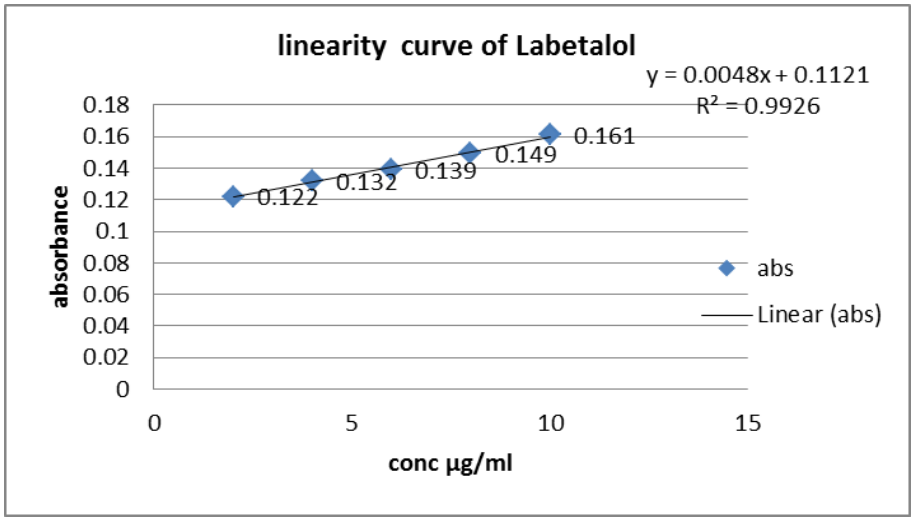

Figure 7: Linearity curve for labetalol HCL at 243.48nm.

Accuracy (Recovery studies)

Accuracy of an analysis was determined methods, recovery study was a carried out by taking the standard mixtures solutions of both Simvastatin and Labetalol HCl (as shown in Table 1).

Table 1: Recovery study data of Simvastatin and Labetalol HCl.[5,9]

Simvastatin(µg/ml)	Labetalol HCl(µg/ml)	Simvastatin (% Recovery)	Labetalol HCl (% Recovery)
2	2	99.83%	99.52%
4	4	99.32%	99.28%
6	6	99.65%	98.65%
8	8	98.59%	96.45%
10	10	98.35%	95.07%

Method precision (Repeatability)

The precision of the instrument was checked by epeated scanning and measurement of absorbance of solutions (n = 3) for Simvastatin and Labetalol HCl (10 µg/ml for both drugs) without changing the parameter of the proposed spectrophotometry method (as shown in Table 2.

Table 2: Regression analysis data.

Parameter	Simvastatin	Labetalol HCl
Wavelength(nm)	239.20 nm	246.00nm
Beer's law limit(µg/ml)	2-10	2-10
Regression Equation (Y= MX + C)	y = 0.010x + 0.024	y = 0.004x+ 0.112
Slope(m)	0.010	0.004
Intercept(c)	0.024	0.112

Correlation coefficient(R^2)	0.999	0.992
Precision(n=3)	9.5	8.0

RESULTS AND DISCUSSION

Q-Absorbance ratio method the primary for developing a method for analysis is that the wavelengths, was fulfilled in case of both these drugs. The two wavelengths were used for the analysis of the drugs were 243.48 nm (iso-absorptive point) and 246 nm (λ-max of Labetalol HCl) at which the calibration curves were prepared for both the drugs. The overlain UV absorption spectra of Simvastatin (239.20 nm) and Labetalol HCl (246.00 nm) showing iso-absorptive point (243.48 nm) in 0.25N NaOH is shown in Figure 5. The validation parameters was study at all the wavelengths for the proposed method.

Accuracy was determined by calculating the recovery and the mean was determined (as shown in Table 1). Precision was calculated as repeatability for both the drugs (as shown in Table 2). Hence, the method can be employed for the routine analysis of these two drugs in combined dosage form.

CONCLUSION

The Spectrophotometer 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 simvastatin and labetalol using Absorbance ratio 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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CONFLICT OF INTREST

Authors do not have any conflict of interest.

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