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Der Pharma Chemica, 2013, 5(3):163-168
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

UV spectrophotometric method for simultaneous estimation of rabeprazole sodium and levosulpiride in bulk and tablet dosage form

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ABSTRACT

A simple, precise and reproducible UV spectrophotometric method, Q-value analysis method, have been developed and validated for the simultaneous estimation ofRabeprazole sodium andLevosulpiride. The method is based on the measurement of absorbance of Rabeprazole sodium and Levosulpirideat 260 nm which is the Isobestic point and 284 nm the λmax of Rabeprazole Sodium. The method obeyed Beer's law in the concentration range of 3-18 µg /ml forRabeprazole sodium and15-90 µg /ml for Levosulpiride. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method. The method was successfully applied to the determination of these drugs in pharmaceutical dosage form.

Keywords: Rabeprazole sodium,Levosulpiride, Q-Analysis method, UV Spectrophotometry.

INTRODUCTION

Rabeprazole sodium (RABE) is a potent proton pump inhibitor that suppress gastric acid secretion by specific inhibition of the gastric H^+, K^+-ATPase enzyme system and thereby suppresses gastric acid secretion.it is used in the treatment of gastrooesophagial reflux disorder (GERD) and duodenal ulcer. Rabeprazole sodium is chemicallyknownas 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl] sulfonic]-1*H*-benzimidazole sodium salt shown in fig-1. [1, 2]

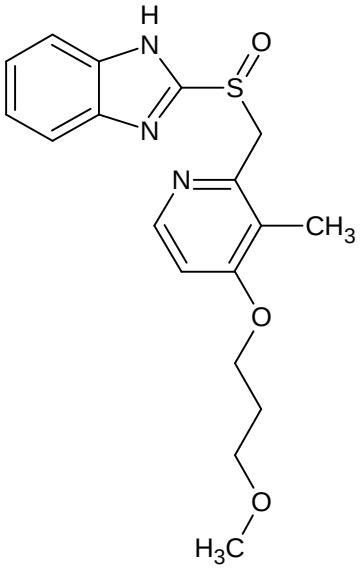

Fig-1: Chemical structure of Rabeprazole sodium

Levosulpiride

Levosulpiride (LEVO) is a Dopamine D2 receptor antagonist .It is an antipsychotic and prokinetic agent. Levosulpiride is also claimed to have mood elevating properties. Levosulpiride is used in the treatment of psychoses, particularly negative symptoms of schizophrenia, anxiety disorders, dysthymia, vertigo, dyspepsia, irritable bowel syndrome and premature ejaculation. It is the (*S*)-enantiomer of sulpiride. Compared with racemic and dextro forms, the levo form of sulpiride has greater anti dopaminergic activity, anti-emetic and antidyspeptic effects and lower acute toxicity. It is chemically known as *n*-{[(2*s*)-1- ethylpyrrolidin-2-yl] methyl}-2-methoxy- 5-sulfamoyl benzamide shown in fig-2.[5,6]

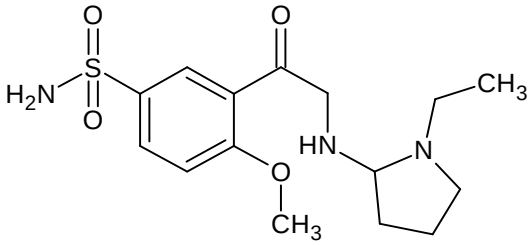

Fig-2Chemical structure of Levosulpiride

In view ofthe need for a suitable method for routine analysis in combinedformulations, attempts are being made to develop simple, preciseand accurate analytical methods for simultaneous estimation oftitle ingredients and extend it for their determination informulation.

MATERIALS AND METHODS

Materials

Levosulpiride (LEVO) and Rabeprazole (RABE) were supplied as a gift sample by Ajantha Pharma Mumbai and Hetero Drugs Limited Hyderabad respectively. Rabekind Plus, a commercial formulation containing a combination of RABE (20 mg) and LEVO (75 mg) manufactured by Qualite Pharmaceuticals,Dehradun was purchased from local firms.All other chemicals used were of pharmaceutical or analytical grade.

Instrumentation

A Jasco double beam UV–visible spectrophotometer, Model: V-630,with a fixed bandwidth (1.5nm) and 1-cm quartz cell was used forSpectral and absorbance measurements. In addition, electronic balance, micropipette and sonicator were used in this study.

Procedure

Preparation of standard stock solution

Standard stock solutions ofRabeprazole sodium and Levosulpiride were prepared by dissolving 25 mg of drug in 25 ml ofmethanol to get standard stock solution of 1000 µg/ml. This solutionwas further diluted to get standard solution of concentration 100µg/ml of RABE and LEVO.

Determination of isoabsorptivepoint and wavelength ofmaximum absorbance

The working standard stock solutions of RABE and LEVOwerescanned in the range of 200 to 400 nm against methanol as a blank.Iso- absorptive point was found at 260 nm.

Preparation of Sample solution from tablet dosage form

For analysis of both RABE and LEVO in tablets, twenty tabletswere accurately weighed and average weight was calculated.Tablets were finely powdered and mixed thoroughly. Quantity of tablet powder equivalent to 20 mg of RABE and 75 mg of LEVOwas weighed accurately, dissolved in 100 ml methanol andsonicated for 20 min. The solution was filtered through Whatman filter paper (No. 41) and transferred to 100 ml volumetric flask and from that solution 1ml was transferred to 10 ml volumetric flask and make up the volume with methanol. The aliquot portion of filtrate was further diluted with methanol to get final concentration of about 4 µg/ml for RABE and 15µg/ml of LEVO.

Calibration curve (Linearity)

A calibration curve was plotted over a concentration range of 3-18 µg/ml for RABE and 15-90 µg/ml for LEVO. Stock solutions forspectrophotometric measurements were prepared by dissolvingRABE and LEVOin methanol to obtain concentration of 1 mg /mlfor each compound. For calibration, series of above solutions wereprepared containing RABE3-18 µg/ml LEVO15-90 µg /mlby diluting the stock standard solution with methanol instandard

volumetric flasks (10ml). Calibration curves wereconstructed for RABE and LEVOby plotting absorbance versusconcentrations at both wavelengths.

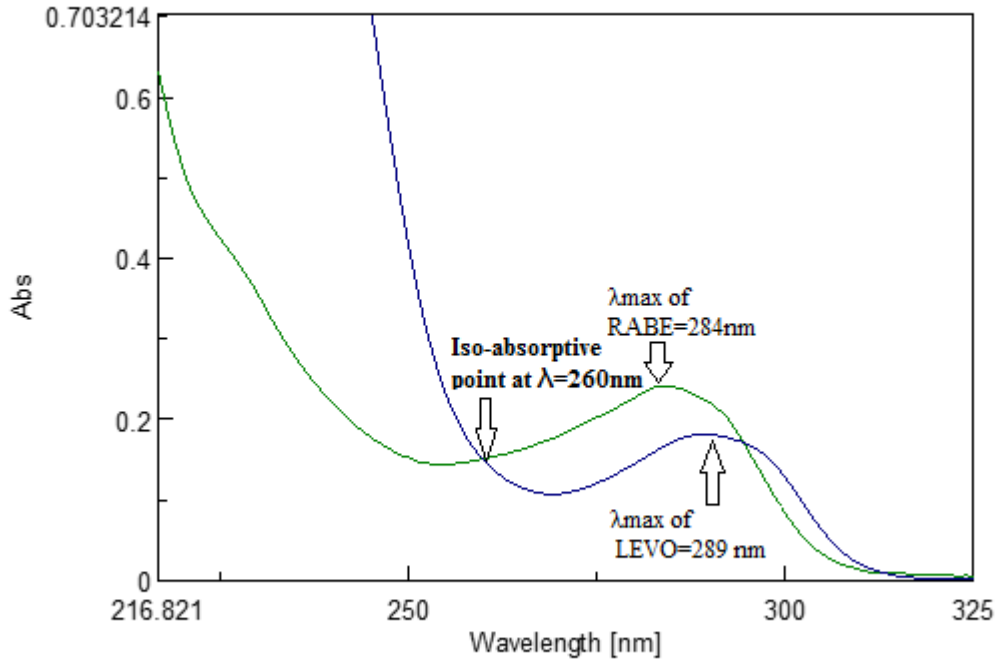

Fig. 3: It shows the overlay spectra of RABE and LEVO showing isoabsorptive point at 260 nm

Table 1: It shows linear regression data for calibration curves.

Parameters	Rabeprazole sodium	Levosulpiride
Linearity range (µg/ml)	3-18	15-90
r^2	0.9995	0.9996
Slope	0.0588	0.037
Intercept	0.0181	0.0002

Q Value Analysis Method

From the overlain spectrum of RABE and LEVOwhich is shown inabove Fig.3, the wavelengths selected for analysis are 260 nm(isobestic point) and 284 nm (λmax ofRabeprazole sodium). Theabsorbance of the standard and sample solutions was measured. Theabsorptivity values for both standard drugs at the selectedwavelengths were employed for determination of Q values .Theconcentrations of drugs in sample solution were determined byusing the following formula. [11]

$$C_X = \frac{(Q_M - Q_Y) \times A_1}{(Q_X - Q_Y) \times aX_1} \quad \text{AND} \quad C_Y = \frac{A_1}{aX_1 - C_X}$$

Where,A_1& A_2 are the absorbance of the mixture at 260 nm & 284 nmrespectively; aX1 and aY1 are absorptivity of RABE and LEVOrespectively at 260 nm; aX_2 and aY2 are absorptivity of RABE and LEVOrespectively at 284 nm; $QM=A_2/A_1$, $QX= aX_2/ aX_1$ and $QY=aY_2/ aY_1$.

Table 2: It shows statistical evaluation of marketed formulation.

Drug	Label claim(mg)	Amount found (mg)	% Label Claim
Rabeprazole Sodium	20 mg	19.7 mg	98.50
Levosulpiride	75 mg	74.2 mg	99.06

Validation of the Developed Method

The methods were validated with respect to linearity,precisionand accuracy.

Linearity

The linearity of an analytical method is its ability to elicit test resultsthat are directly or by a well-defined mathematical transformationproportional to the concentration of analyte in samples within agiven range. The range of analytical method is the interval betweenupper and lower level of analyte including levels that have beendemonstrated to be determining with precision and accuracy usingthe method. The linear response of RABE and LEVO weredetermined by analysing five independent levels of the calibrationcurve in the range of 3-18 µg/ml for RABE and 15-90 µg/ml for LEVO. Result should be expressed in terms of Correlation co-efficient.

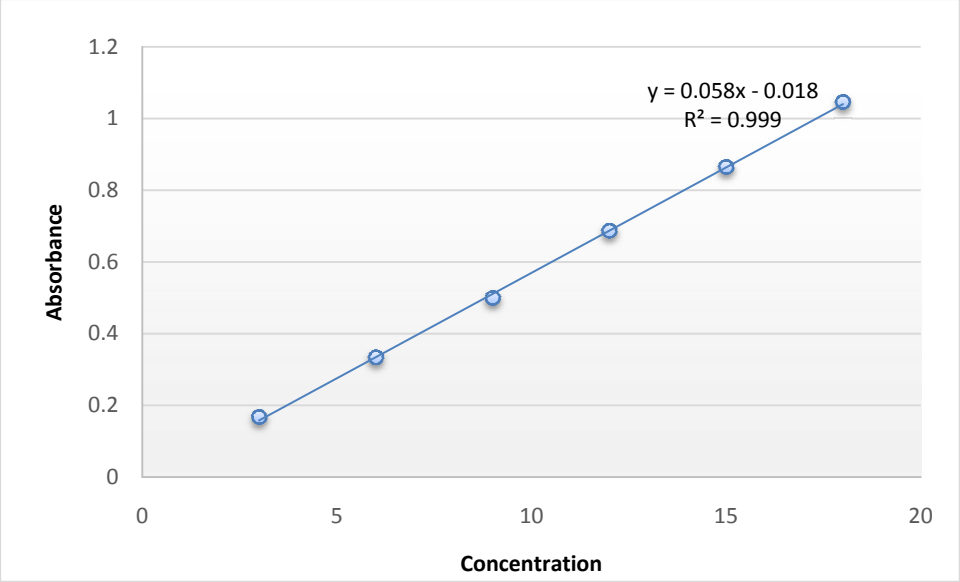

Fig. 3: It shows calibration curve of RABE

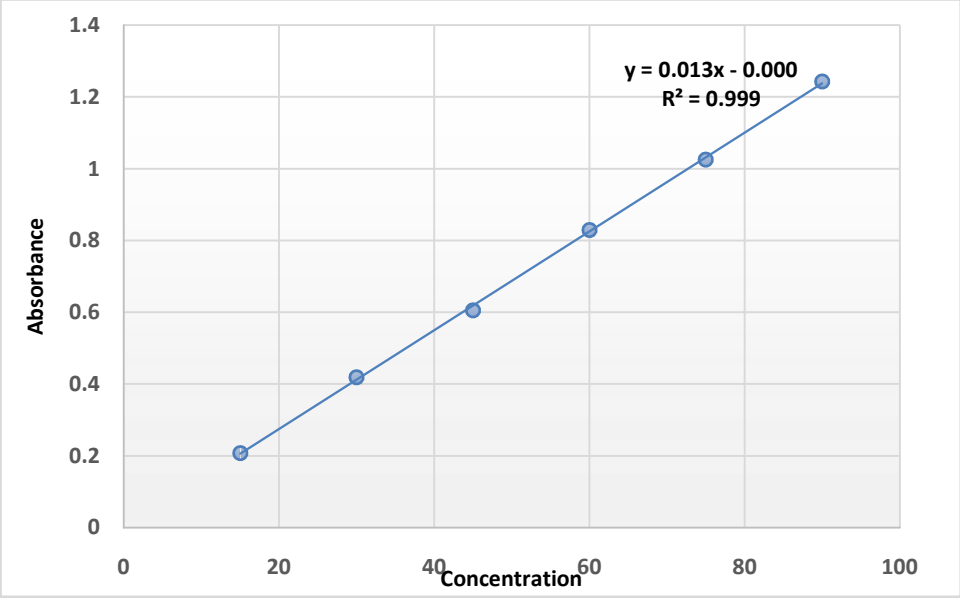

Fig. 4: It shows calibration curve of LEVO

Precision

The reproducibility of the proposed method was determined byperforming tablet assay at different time intervals (morning,afternoon and evening) on same day (Intra-day assay precision) andon three different days (Inter-day precision). Result of intra-day andinter-day precision is expressed in % RSD.

Table 3: It shows result of Intraday and Interday precision

Drug	% RSD (intra day)	% RSD (inter day)
Rabeprazole sodium	0.4896	0.8908
Levosulpiride	0.47027	0.7490

Accuracy (% Recovery)

Accuracy of an analysis is determined by systemic error involved. Itis defined as closeness of agreement between the actual (true) valueand analytical value and obtained by applying test method for anumber of times. Accuracy may often be expressed as % Recoveryby the assay of added amount of analyte. It is measure of theexactness of the analytical method. Recovery studies carried out forboth the methods by spiking standard drug in the powderedformulations 80%, 100%, 120% amount of each dosage content as per ICH guidelines.

Table 4: It shows result of Recovery study

Recovery Level (%)	Drug	Conc. of drug (µg/ml)		% Recovery
		Drug Taken	**Std. drug added**	
80		4	3.2	99.65
100	RABE	4	4.0	99.47
120		4	4.8	99.48
80		15	12	99.32
100	LEVO	15	15	100.30
120		15	18	99.80

RESULTS AND DISCUSSION

In this method, the standard stock solutions of RABE and LEVOwere prepared in methanol.The Calibration curves for RABE(3-18 µg /ml) and LEVO (15-90 µg /ml) were plotted and molar absorptivity for boththe drugs were calculated at both the wavelengths of 284 nm (λmax ofRABE) and 260 nm (isoabsorptive point). It is evident from thespectra of RABE and LEVOthat these drugs obey the Lambertbeer'slaw at all the wavelength. The regression characteristics arereported in Table no.1. The assay was performed by measuringabsorbance of the sample solutions at respective wavelengths forthe formulation calculating Q-values for the drugs and then putthese values in formula and determined content of each drug informulation. The result of assay is reported in Table no.2. Recoverystudies were carried out by spiking standard drug in the powderedformulations in 80%, 100%, 120% amount of each drug as per ICHguidelines. The results of the recovery analysis are reported in Table4 which proved the good accuracy of the proposed methods.

Acknowledgement

Authors are thankful toAjantha Pharma, Mumbai and Hetero Drugs Ltd. Hyderabad,for providing the gift samples of Levosulpiride and Rabeprazole sodium forcarrying the research work.The authors are also thankful to the management, Sinhgad Technical Education Society's, Smt. Kashibai Navale College of Pharmacy, Kondhwa (Bk.), Pune-48, for providing excellent research facilities

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