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Simultaneous estimation of rabeprazole sodium and levosulpiride by UV-spectrophotometry in tablet formulation

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ABSTRACT

A new, simple, economic, rapid and novel spectrophotometric method has been developed for simultaneous estimation of Rabeprazole Sodium (RAB) and Levosulpiride LEV. Simultaneous equation method is used. The method involves measurement of absorbance at wavelengths, 284 nm and 232 nm, λ_{max} of RAB and LEV respectively. RAB and LEV obeys Beer's law obeyed in concentration range of 4-24 µg/ mL and 15-45 µg/ mL respectively. The proposed method is recommended for routine analysis since it is rapid, simple, accurate, precise, sensitive and specific. This paper describes the development and validation of UV spectroscopic method for Simultaneous estimation of RAB and LEV in combined tablet dosage form.

INTRODUCTION

Development of the simple and reproducible analytical methods for estimation of multicomponent drugs is very important part of quality control and assurance. Multicomponent formulations in market are increasing. It is very essential that two or more number of drugs should be estimated simultaneously[1].

Rabeprazole sodium is 2 - [[[4 – (3 –methoxy – propoxy) – 3 – methyl 2 – pyridinyl] methyl] sulfinyl] – 1H – benzimidazole sodium salt. Rabeprazole sodium (RAB) is proton pump inhibitor belongs to a class of antisecretory compounds. Suppress gastric acid secretion by inhibiting the gastric H^+/K^+ ATPase at the secretory surface of the gastric parietal cell[2].

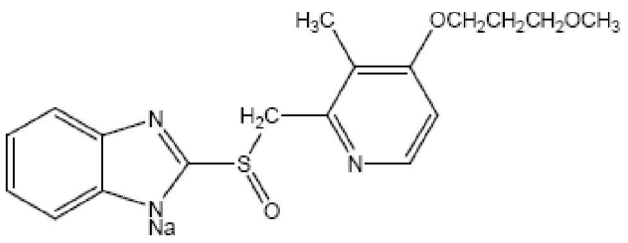

Figure 1 : 2 - [[[4 – (3 –methoxy – propoxy) – 3 – methyl 2 – pyridinyl] methyl] sulfinyl] – 1H – benzimidazole sodium

Levosulpiride, a purified levo isomer of sulpiride, chemically it is 5 (aminosulfonyl) N [(1 ethyl 2 pyrrolidinyl)methyl] 2 methoxy benzamide. LEV is a D2 dopamine receptor antagonist and commonly prescribed to patients with functional dyspepsia, psychosis, and depression. At low doses, LEV increases Dopaminergic neurotransmission primarily by the blocking of the dopamine autoreceptors which inhibits the pre synaptic dopamine synthesis and release of dopamine. Compared with racemic and dextro forms, the levo

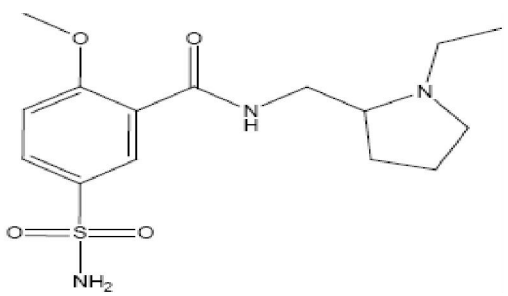

Figure 2 : 5-(aminosulfonyl)-N-[(1-ethyl-2-pyrrolidinyl) methyl]-2-methoxy benzamide

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form of sulpiride has greater central antidopaminergic activity4, antiemetic and antidyspeptic effects and lower acute toxicity[3].

MATERIALS

Pharmaceutical grade Rabeprazole and Levosulpiride were pursued as a gift sample from Enal Drugs Pvt. Ltd. Jedimetla Hyderabad (A.P.) All chemicals and solvents of AR grade and were purchased from Qualigens fine Chemicals, Mumbai, India.

UV- spectrophotometer UV-1800 (Shimadzu, Japan) with spectral bandwidth of 2 nm and 10 mm matched quartz cells were used for development analytical method over the range of 200-400 nm.

Marketed formulation Rabekind Plus tablet containing RAB 20 mg and LEV 75 mg was used as sample; purchased from local pharmacy. Calibrated glassware's were used throughout the work.

PROCEDURE

Method used for simultaneous estimation of rab and lev

The drug RAB (20mg) and LEV (15mg) were separately dissolved in Methanol to get 200µg/ml and 150 µg/ml solution respectively. Further diluted with methanol and scanned for maximum absorbance (λmax) in a UV-VIS Spectrophotometer between a U.V range from 200 to 400 nm against methanol as blank.

For estimation of both the drugs, the wavelength maxima of RAB and LEV were determined and found to be 284 nm (λ1) and 232nm (λ2) respectively where there was no interference among the drugs. Calibration curve was plotted between absorbance and its nominal concentration in the range of 0-24 µg/ml for RAB and 0-45 µg/ml for LEV at their respective maxima.

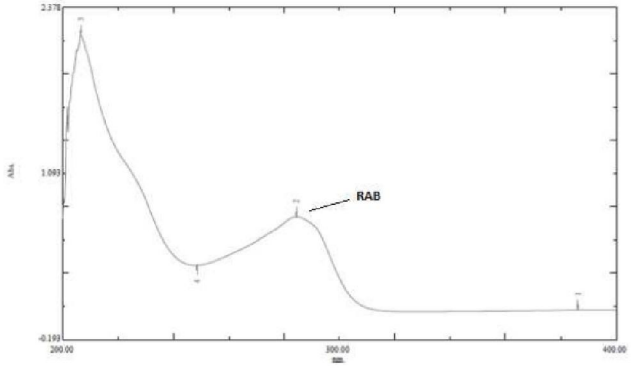

Figure 3 : Absorbance spectrum of RAB

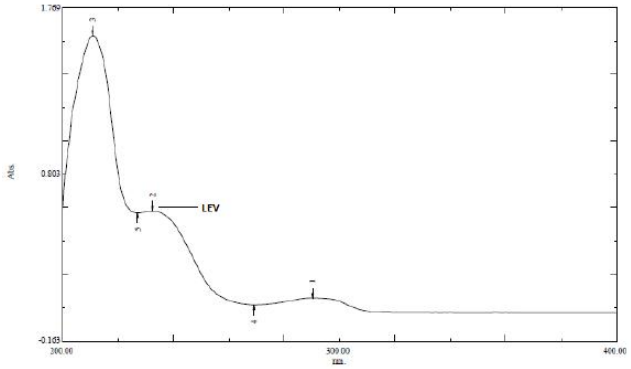

Figure 4 : Absorbance spectrum of LEV

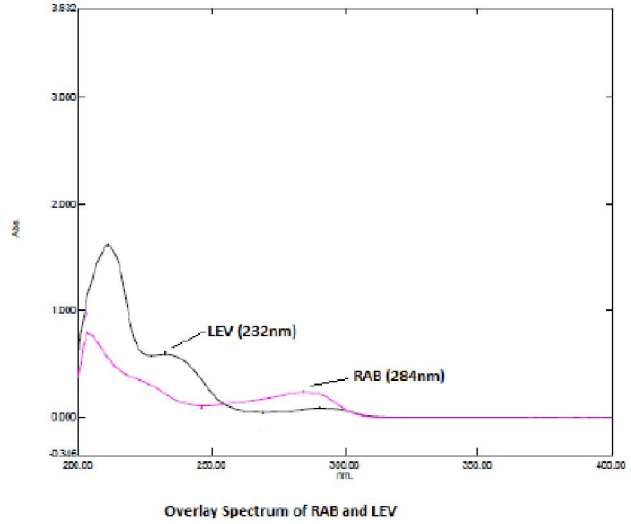

Figure 5 : Overlay spectrum of RAB and LEV

Calibration curve of rab and lev

Stock solutions of RAB and LEV were prepared by dissolving 20 mg of RAB and 15mg LEV separately dissolved in methanol and then the volume was adjusted to 100 ml with methanol separately.

Stock solutions of RAB and LEV were subse-

TABLE 1 : Linearity study of RAB

Sr.No.	Concentration (µg/ml)	Absorbance (nm)	Regression Data		
1	4	0.192			
2	8	0.376			
3	12	0.573	m=	c= -	r^2=
4	16	0.759	0.048	0.002	0.997
5	20	0.99			
6	24	1.131			

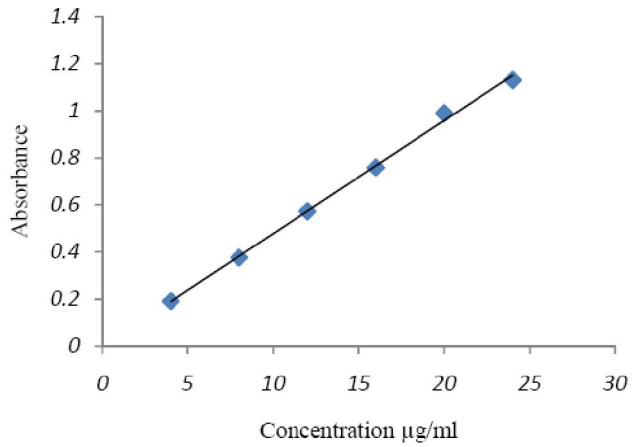

Figure 6 : Caliberation curve for RAB

TABLE 2 : Linearity study of LEV

Sr.No.	Concentration (µg/ml)	Absobance (nm)	Regression Data		
1	5	0.333			
2	10	0.596			
3	15	0.907			
4	20	1.186	m= 0.059	c= 0.003	r^2= 0.998
5	25	1.514			
6	30	1.734			
7	45	2.741			

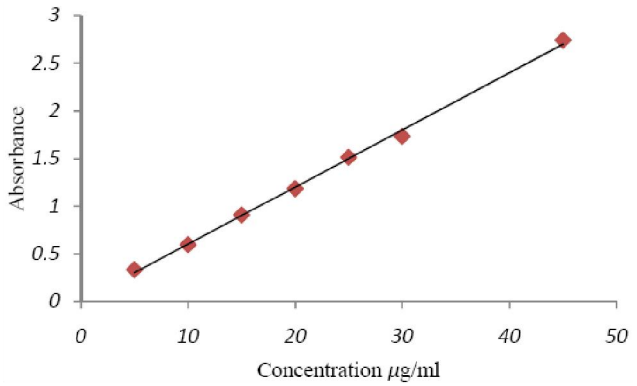

Figure 7 : Caliberation Curve for LEV

quently diluted with methanol to get 4, 8, 12, 16, 20, 24 µg/ml and 5, 10, 15, 20, 25, 30, 45 µg/ml respectively. Then the absorbance of these diluted solutions were measured at 284 nm (λ1) for RAB and 232nm (λ2) for LEV by using double beam U.V. spectrophotometer against a blank of methanol. Average of six replicates readings was taken and tabulated. Regression equation was derived from the slope of the curve Y= 0.048X-0.002; r^2 = 0.997 for RAB. For LEV regression equation is Y=0.059X; r^2 = 0.99.

Preparation of sample solution

Twenty tablets were accurately weighed and crushed to fine powder. Powder equivalent to 16 mg of RAB and 60mg of LEV was weighed and dissolved in methanol, sonicated for 20 min and filtered. After rejecting first few ml, different concentrations of tablet sample were prepared by serial dilution technique and used for analysis.

Method validation

The method validation parameters linearity, precision, accuracy, repeatability, limit of detection and limit of quantitation were checked as per ICH guidelines.

Linearity and range

The linearity for RAB and LEV were determined at six concentration levels, ranging from 4-24 µg/ml and 15-45 µg/ml respectively using working standards.

Precision and accuracy

The precision of the method was evaluated by Interday and Intraday variation studies. In intraday studies, working solutions of standard and sample were analysed thrice in a day and percentage relative standard deviation (% RSD) was calculated. In the interday variation studies, working solution of standard and sample were analysed on two consecutive days and percentage relative standard deviation (% RSD) was calculated. The data is shown in TABLE 4

TABLE 3 : Result of tablet formulation

Drug	Labeled amt. (mg)*	Estimated amt. (mg)*	% Estimation*	±S.D. *	%RSD*	COV*	S. E. *
RAB	20	19.945	99.726	0.869	0.871	0.295	0.857
LEV	75	74.93	99.907	0.593	0.593	0.071	0.622

***mean of six determinations**

Limit of detection and limit of quantitation

The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula and shown in TABLE 4.

TABLE 4 : Summary of validation parameters for dual wavelength method

Parameters		RAB	LEV
Linearity Range (μg/ml)		4-24	15-45
Correlation coefficient (r^2)		0.997	0.998
Precision (RSD)	Intraday*	0.9861	0.5619
	Interday*	0.5967	0.5535
Accuracy (%)	80%@	99.761 ± 0.766	100.011 ± 0.864
	100%@	99.686 ± 0.667	99.736 ± 0.447
	120%@	99.733 ± 0.414	99.976 ± 0.820
Repeatability (RSD)*		0.731019	0.539208
LOD (μg/ml)		0.158	0.195
LOQ (μg/ml)		0.481	0.592

***Six Determinations, @ Three Determinations, RSD-Relative Standard Deviation**

LOD = 3.3 (σ / S)

Where, S = slope of calibration curve, σ = standard deviation of the response. The Limit of Quantification (LOQ) is the smallest concentration of the analyte, which gives a response that can be accurately quantified. LOQ was calculated using the following formula and shown in TABLE 4.

LOQ = 10 (σ / S)

Where, S = slope of calibration curve, σ = standard deviation of the response.

RESULTS AND DISCUSSION

In the present work, new simultaneous estimation method was developed for the simultaneous spectroscopic estimation of RAB and LEV in commercially available tablet dosage form.

The concentrations in the range of 4-24 μg/ml of RAB and 15-45 μg/ml of mixed working standard and two set of wavelengths gave optimum accuracy, precision, time, economy, and sensitivity for this method. The proposed procedure was successfully applied to the determination of RAB and LEV in the commercially available tablets dosage form, and the results are shown in TABLE 3.

The recovery studies were carried out at different concentrations by spiking a known concentration of standard drug to the pre-analyzed sample and contents were reanalyzed by proposed methods. The method was validated statistically for range, linearity, precision, accuracy, repeatability, LOD, and LOQ (TABLE 4). Accuracy was ascertained on the basis of recovery studies. Precision was calculated as interday and intraday variation for both the drugs. The contents estimated using the proposed method was found in agreement with the labeled amount. The relative standard deviations were found to be within the limit, indicating good accuracy, precision, and repeatability of the proposed method.

CONCLUSION

The simultaneous estimation method permits simple, rapid and direct determination of RAB and LEV in commercially available tablet dosage form without previous separation. The results of analysis of two drugs from tablet formulation using method was found close to 100%, Standard deviation was satisfactorily low indicating accuracy and reproducibility of the method. Recovery studies were satisfactory which showed that there is no interference of excipients.

The most striking feature of this method is its simplicity and rapidity, non- requiring- consuming sample preparations such as extraction of solvents, heating, degassing which are generally needed for HPLC analysis. It is a new and novel method and can be employed for routine quality control analysis. The described method gives accurate and precise results for determination of RAB and LEV in tablets.

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