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تطبيقات لطريقة المعادلة المتزان وطريقة المشتقة لتحديد راببيرازول صوديوم وليفوسلبيراييد في الجرعات الدوائية وانهال العينات

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المخلص:

في هذه الدراسة، تم تطوير طريقتين طيفيتين بسيطتين ودقيقتين غير مكلفتين وغير مملتين للتقدير المتزامن للدوائين لراببيرازول صوديوم وليفوسلبيراييد في الاقراص الدوائية المركبة. استندت الطريقة الأولى على توظيف طريقة المعادلة المتزامن لتحليل دوائي الراببيرازول صوديوم والليفوسلبيراييد الذين أعطيا قمم للامتصاص عند الاطوال الموجية 284 و 232 نانوميتر على التوالي في مذيب الميثانول. اما الطريقة الثانية فقد استندت على تعيين الدوائين بطريقة الإشتقاق الطيفي التي تنطوي على تحديد نقطة التقاطع الصفريّة. تم إجراء طيف الإشتقاق الأول في الميثانول وإجراء القياسات عند 231.2 نانوميتر (نقطة تقاطع ليفوسلبيراييد الصفريّة) لدواء راببيرازول صوديوم وعند 246.2 نانوميتر (نقطة تقاطع راببيرازول صوديوم الصفريّة) لدواء ليفوسلبيراييد. لقد لوحظ بان استجابة الدوائين كانت خطية في مدى التراكيز 1-20 ميكروجرام/مل. أما وسط انهال الدوائين المستخدم كان 900 مل من المحلول المنظم (أس هيدروجيني 7.4) باستخدام جهاز USP نوع 2 عند سرعة تحريك 100 دورة في الدقيقة. وتم قياس الدواء المتحرر بطرق طيفية متقدمة. ولقد تم البرهان على ملائمة الطريقة المطورة هذه للتعين الكمي لدوائي الراببيرازول صوديوم والليفوسلبيراييد من خلال إخضاعها لعملية تحقق.



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ORIGINAL ARTICLE

Applications of simultaneous equation method and derivative method for the determination of rabeprazole sodium and levosulpiride in pharmaceutical dosage form and dissolution samples



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KEYWORDS

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method;
Derivative spectrophotometry;
Dissolution

Abstract Two simple, accurate, precise, economical procedures, entailing neither irksome sample treatment nor tedious extraction process have been developed for the simultaneous estimation of rabeprazole sodium and levosulpiride in combined tablet dosage form. The first method was based on employing simultaneous equation method for analysis of both drugs. Rabeprazole sodium and levosulpiride have shown absorbance maxima at 284 and 232 nm in methanol, respectively. The second method was based on derivative spectrophotometric method involving the determination of both the drugs at their respective zero crossing point (ZCP). The first order derivative spectrum was obtained in methanol and the determinations were made at 231.2 nm (ZCP of levosulpiride) for rabeprazole sodium and 246.2 nm (ZCP of rabeprazole sodium) for levosulpiride. The linearity was obeyed in the concentration range of 1–20 µg/ml for both drugs. The medium of dissolution was used 900 ml of phosphate buffer pH 7.4 using a USP type 2 apparatus at a stirring rate of 100 rpm. The drug release was evaluated by developed spectroscopic methods. The suitability of the developed method for quantitative determination of rabeprazole sodium and levosulpiride was proved by validation.

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1. Introduction

Chemically, rabeprazole sodium (RAB) is 2-([4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methanesulfonyl)-1H-benzimidazole sodium salt (Indian Pharmacopoeia, 2010; Merck Index, 2003) (Fig. 1) is a class of antisecretory compounds that selectively inhibits gastric acid secretion by inhibiting the H⁺ and K⁺ ATPase at secretory surface of the gastric parietal cell

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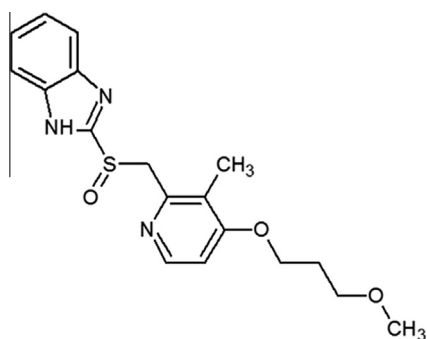


Figure 1 Structure of rabeprazole sodium.

(Tripathi, 2003). It has been shown to be effective for the treatment of gastric and duodenal ulcers and for gastro-esophageal reflux disease (GERD) (Swan et al., 1999).

Levosulpiride (LEV) is a levo-enantiomer of racemic sulpiride belonging to the substituted benzamide group. Chemically it is 5-(aminosulfonyl)-N-[(1-ethyl-2-pyrrolidiny)methyl]-2-methoxybenzamide (Fig. 2) (Merck Index, 2003). It is a typical neuroleptic drug with sulpiride and inhibits dopaminergic D2 receptors at the trigger zone both in the central nervous system and in the gastrointestinal tract as stated (Barbeau, 2008).

Combination of rabeprazole sodium and levosulpiride is available in the market which is used to help to reduce such as the amount of acid produced by the stomach and improve gastrointestinal motility and to treat conditions such as heartburn, GERD and gastritis (Swan et al., 1999). Once rabeprazole has left the stomach, absorption occurs within 1 h of administration. The bioavailability is approximately 52%. Due to low solubility, oral formulations of levosulpiride suffer from low absorption in the gastrointestinal tract thus resulting in lower bioavailability. Orally administered levosulpiride is absorbed from upper portion of the small intestine (Barbeau, 2008).

Drug dissolution (or release) testing is an analytical technique used to assess release profiles of drugs in pharmaceutical products, generally solid oral products such as tablets and capsules (United States Pharmacopeia, 2009; Brown, 2005). This test gains its significance from the fact that if a drug from a product is to produce its effect; it must be released from the product and should generally be dissolved in the fluids of the gastrointestinal (GI) tract. Thus, a drug dissolution test may be considered as an indicator of potential drug release and absorption characteristics of a product in humans as well as

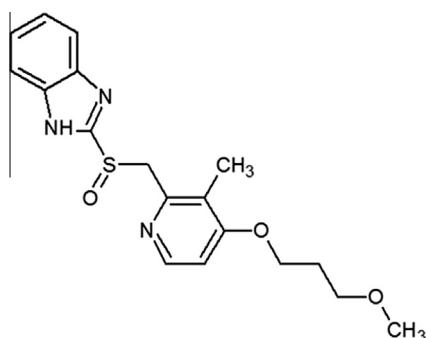


Figure 2 Structure of levosulpiride.

in animals. Therefore, a dissolution test is often considered a surrogate for the assessment of availability of drugs in the body, generally termed bioavailability (Siewert et al., 2003; Swartz, 2011).

RAB is official in Indian Pharmacopoeia which includes HPLC assay method. The literature reports many analytical methods like spectrophotometry (Gunji et al., 2012; Rahman et al., 2008), chromatography (Bharathi et al., 2009; Choudhary et al., 2009), Thin layer chromatography and High performance thin layer (Osman and Osman, 2009; Suganthi et al., 2008) and dissolution method (Garcia et al., 2006) for estimation of Rabeprazole sodium alone or in combination with other drugs. LEV is not official in any pharmacopoeia. Analytical methods like spectrophotometry (Manjunath et al., 2011), stability indicating HPLC and HPTLC (Naguib and Abdelkawy, 2010), and chromatography (Walash et al., 2012) for the determination of levosulpiride alone or in combination with other drugs have been reported.

Simultaneous estimation of RAB and LEV in combined dosage form by UV-spectrophotometric methods (Pekamwar et al., 2013; Bhalodia et al., 2012) and HPLC (Patel et al., 2012; Sirisha and Ravikumar, 2012; China Raju et al., 2012; Agarwal and Jagdigsh, 2012) has been reported in the literature. The reported UV method (Pekamwar et al., 2013) describes only direct simultaneous estimation of RAB and LEV at mentioned wavelengths.

The authors did not consider interference in quantitation of one drug due to absorption of other drugs at same wavelength. Another reported method (Bhalodia et al., 2012) was absorbance ratio method for simultaneous spectroscopic estimation of RAB and LEV.

In the present work, two simple UV spectrophotometric methods for simultaneous estimation of rabeprazole sodium and levosulpiride in combined dosage form and its application to determination of dissolution sample were reported. These methods were validated according to the ICH Q2 (R1) guidelines ICH (2005).

2. Experimental

2.1. Materials and reagents

Rabeprazole sodium and levosulpiride bulk drugs were obtained from Torrent Pharma. Pvt. Ltd, Gujarat, India, as gift samples. Methanol (AR Grade) was purchased from Merck (India) Ltd., Mumbai, India. AR grade chemicals and distilled water were used during experimentation. Commercial pharmaceutical preparation (Rabekind Plus®, Mankind Pharma, New Delhi) was procured from the local pharmacy shop, containing 20 mg of rabeprazole sodium and 75 mg of levosulpiride (extended release).

2.2. Instrumentation

A UV-Visible spectrophotometer (Shimadzu-1700, UV Probe 2.21 software) with a spectral bandwidth of 1 nm was employed for all spectroscopic measurements, using a pair of 1.0 cm matched quartz cells over the range of 200–400 nm. The USP dissolution apparatus Electrolab TDT-08L, was used for dissolution study. The Elico Li 614 pH analyzer was used to determine the pH of dissolution media, deaerated by

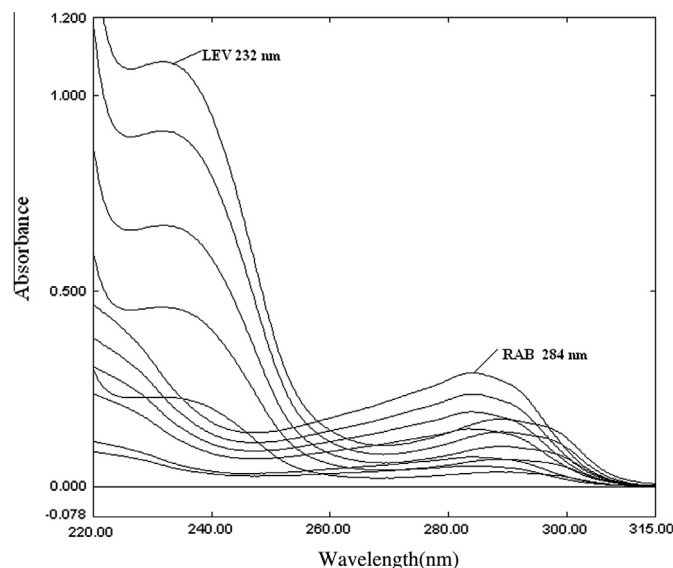


Figure 3 Overlain zero order spectra of RAB (3 µg/ml) and LEV (12 µg/ml).

vacuum filtration and was maintained at 37.0 ± 0.5 °C by using a thermostatic bath.

2.3. Selection of common solvent

Methanol was selected as common solvent for studying spectral characteristics of the selected drugs.

2.4. Preparation of standard stock solutions

Stock standard solutions of RAB and LEV were separately prepared by dissolving 10 mg in 100 ml volumetric flask containing 50 mL methanol and the volume was made up to the mark with methanol to obtain concentrations of 100 µg/mL each.

2.4.1. Method I: simultaneous equation method

Appropriate volume, 0.3 mL of RAB and 1.2 ml LEV standard stock solution was transferred to two separate 10 mL volumetric flasks and the volume was adjusted to mark with methanol to get concentration 3 and 12 µg/mL, respectively. The solutions were scanned separately in the UV-region i.e. 400-200 nm. From the overlain spectra (Fig. 3) two wavelengths, 284 nm (λ_{\max} of RAB) and 232 nm (λ_{\max} of LEV) were selected for the formation of simultaneous equation. The A (1%, 1 cm) was determined at both the wavelengths selected for each drug. A set of two simultaneous equations was formed as:

$$C_x = \frac{(A_2 a_{y_1} - A_1 a_{y_2})(A_2 a_{y_1} - A_1 a_{y_2})}{(a_{x_2} a_{y_1} - a_{x_1} a_{y_2})} \quad (1)$$

$$C_y = \frac{(A_1 a_{x_2} - A_2 a_{x_1})(A_1 a_{x_2} - A_2 a_{x_1})}{(a_{x_2} a_{y_1} - a_{x_1} a_{y_2})} \quad (2)$$

where,

A_1 and A_2 are the absorbance of sample solutions at 284 and 232 nm, respectively.

a_{x_1} and a_{x_2} (490, 473.0) are E (1%, 1 cm) of RAB at 284.0 and 232.0 nm.

a_{y_1} and a_{y_2} (77.5, 560.0) are E (1%, 1 cm) of LEV at 284.0 and 232.0 nm.

C_x and C_y are concentrations of rabeprazole sodium and levosulpiride in mg/mL in sample solution. The values of C_x and C_y were calculated by putting the values of A_1 and A_2 to solve the simultaneous Eqs. 1 and 2 (Patel and Patel, 2008).

2.4.2. Method II: derivative spectrophotometric method

Appropriate volume, 0.3 mL of RAB and 1.2 ml LEV standard stock solution was transferred to two separate 10 mL volumetric flasks and the volume was adjusted to mark with methanol to get concentration 3 and 12 µg/mL, respectively. The solutions were scanned separately in the UV-region i.e. 400-200 nm. The zero-order spectrum was processed to obtain first-derivative spectrum (Patel and Patel, 2008; Dave et al., 2007). The two first derivative spectra were overlaid which shows that RAB showed zero crossing at 246.2 nm, while LEV showed zero crossing at 231.2 nm. The determinations were made at 231.2 nm for RAB (ZCP of LEV) and 246.2 nm for LEV (ZCP of RAB). The zero order and first order overlaying spectra are presented in Figs. 3 and 4, respectively.

2.5. Assay of tablet formulation

Twenty tablets were accurately weighed and crushed. A quantity of tablet powder equivalent to 10 mg of RAB was transferred to 100 ml volumetric flask and dissolved in methanol, sonicated for 20 min and the volume was made to 100 ml with the same solvent. The solution was filtered and was further diluted to get a final concentration of about 2 µg/mL RAB and 7.5 µg/mL of LEV. The response of sample solutions was measured at 232.0 and 284.0 nm for simultaneous equation method and at 231.2 and 246.2 nm for first derivative method in 1 cm cell against blank. The content of RAB and LEV in tablet dosage form was calculated using two framed simultaneous equations and derivative method.

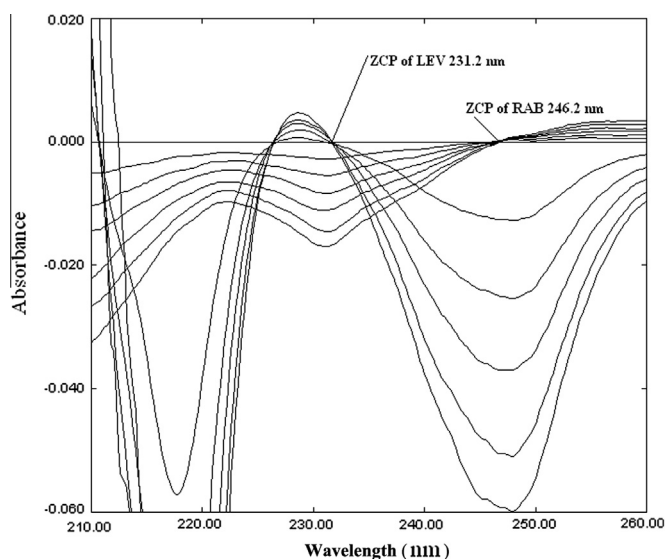


Figure 4 Overlain 1st derivative spectra of RAB (3 µg/ml) and LEV (12 µg/ml).

2.6. Comparison with the reported method

A quantity of tablet powder equivalent to 10 mg of rabeprazole was transferred to 100 ml volumetric flask and dissolved in methanol, sonicated for 20 min. and the volume was made up to mark with methanol. The solution was filtered through whatman filter paper No. 41. The aliquot portion of filtrate was further diluted to get a final concentration of about 2.0 µg/ml of rabeprazole and 7.5 µg/ml of levosulpiride. The samples were analyzed by optimized spectroscopic method and the reported HPLC method. The results of proposed spectrophotometric methods were compared with the reported RP-HPLC method (China Raju et al., 2012).

2.7. Dissolution study

Dissolution testing was carried out using paddle (USP Apparatus 2) at 50 rpm using 900 ml of 0.1 N HCl as dissolution medium for 2 h. Further, the profile was determined using 900 ml phosphate buffer pH 7.4 at 100 rpm for 24 h. Sampling aliquots of 5.0 ml were withdrawn at intervals of 5, 10, 15, 30, 45, 60, 90 and 120 min and later after every two hours up to 24 h and replaced with an equal volume of the fresh medium to maintain a constant total volume. After the end of each test time, sample aliquots were filtered, diluted with methanol and quantified. The analysis of dissolution samples was performed using simultaneous equation method and first derivative spectrophotometric method. The proposed methods were employed to calculate the percentage release on each time of dissolution profile.

3. Method validation

The method was validated according to the ICH Q2 (R1) guidelines for validation of analytical procedures for parameters like linearity, precision, accuracy, LOD, LOQ and specificity for the analyte.

3.1. Linearity

Aliquot portions 0.1-2.0 mL of RAB & LEV were separately transferred into 10 mL volumetric flasks. The volume was adjusted to the mark with methanol to obtain concentrations 1-20 µg/mL of RAB and LEV. For method I, absorbance of these solutions was measured at 284.0 nm and 232.0 nm for RAB and LEV, respectively. For method II, the amplitudes from the first order spectra were recorded at 231.2 and 246.2 nm for RAB and LEV, respectively. Calibration curve was constructed by plotting response versus concentration.

3.2. Accuracy

To ascertain the accuracy of the proposed methods, recovery study was carried out by standard addition method at three different levels (80%, 100% and 120%).

The % recovery by proposed method was calculated using the formula as below.

$$\text{Recovery} = (A-B)/C \times 100 \quad (3)$$

where

A = Total amount of drug estimated (mg).

B = Amount of drug found on pre-analyzed basis (mg).

C = Amount of bulk drug added (mg).

3.3. Precision

Precision was studied to find out intra and inter-day variations in the test method of RAB and LEV. Calibration curves prepared in medium were run in triplicates on the same day and for three days at three different concentration levels and % RSD (relative standard deviation) was calculated.

3.4. Limit of detection and limit of quantitation

The limit of detection (LOD) and the limit of quantification (LOQ) of the drug were derived by calculating the signal-to-

noise ratio (S/N , i.e., 3.3 for LOD and 10 for LOQ) using the following equations designated by the International Conference on Harmonization (ICH).

$$\text{LOD} = 3.3 \times \sigma/S \quad (4)$$

$$\text{LOQ} = 10 \times \sigma/S \quad (5)$$

where,

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

3.5. Specificity study

Specificity of method was checked by estimating drug in the presence of excipients such as lactose, starch and magnesium stearate which are mostly available in tablet formulation. The drug-excipient samples were prepared by considering low and high ratio of excipient in the formulation. The drug-excipient blend was used to prepare working standard solution of a final concentration of about 2 $\mu\text{g/mL}$ RAB and 7.5 $\mu\text{g/mL}$ of LEV. The samples were analyzed by optimized spectroscopic methods and the recovery value was calculated.

4. Results and discussion

In the present study, we tried to develop spectroscopic methods for the simultaneous estimation of RAB and LEV from pharmaceutical dosage form. Another aspect of the study was to check applicability of the developed spectroscopic methods for the determination of dissolution samples. The two simple spectroscopic methods were developed for simultaneous estimation of RAB and LEV from their pharmaceutical dosage form. The developed simultaneous equation method and first order derivative spectroscopic method were also used to determine the dissolution samples. The developed methods were validated as per the ICH guidelines for different parameters.

4.1. Optimization of spectroscopic methods

RAB and LEV were soluble in methanol and were used as solvents for the spectroscopic study.

4.2. Simultaneous equation method

As the overlay spectrum of RAB and LEV (Fig. 3) shows that there was interference in quantitation of individual drug at their λ_{max} due to absorption of another drug at that particular wavelength. So, the simultaneous equation method was developed for estimation of RAB and LEV from the pharmaceutical dosage form.

4.3. First derivative spectroscopic method

Another option thought for the simultaneous estimation of RAB and LEV which avoids interference due to other drugs in combination (Fig. 3) and interference due to excipient was the first derivative spectroscopic method.

4.4. Validation of spectroscopic methods

The developed simultaneous equation method and first derivative spectroscopic method were validated as per the ICH validation guidelines.

4.5. Linearity

Linear relationship was found in the concentration range of 1–20 $\mu\text{g/mL}$ for RAB and LEV by both methods and results are shown in (Table 1).

4.6. Precision

The results of intra-day and inter-day precision were expressed as % RSD and it was found to be NMT 2. The results of intra and inter day precision are shown in (Table 1).

4.7. Accuracy

The recovery studies were carried out at three levels and three determinations were made at each levels and percentage recovery was calculated. From the data obtained, it was observed that the recovery of standard drugs RAB and LEV was accurate and within the limits employing both methods. The results are mentioned in (Table 2).

Table 1 Optical characteristics and validation of proposed method.

Parameters	Method I		Method II	
	RAB	LEV	RAB	LEV
λ_{max}	284 nm	232 nm	231.2 nm	246.2 nm
Linearity range	1–20 $\mu\text{g/ml}$	1–20 $\mu\text{g/ml}$	1–20 $\mu\text{g/ml}$	1–20 $\mu\text{g/ml}$
Correlation coefficient	0.9992	0.9981	0.9982	0.9998
Slope	0.0465 \times	0.0542 \times	0.0033 \times	0.0031 \times
Limit of detection ($\mu\text{g/ml}$)	0.112	0.136	0.081	0.319
Limit of quantification ($\mu\text{g/ml}$)	0.340	0.413	0.24	0.968
Precision (% RSD)				
i. Intraday precision	1.10	0.48	1.03	1.37
ii. Interday precision	1.25	0.52	1.16	1.53
% Recovery	99.45	98.34	99.21	99.23
Specificity	Specific	Specific	Specific	Specific

Table 2 Results of accuracy study.

Drugs	Label claim (mg)	% Excess drug added	% Recovery		% RSD	
			Method I	Method II	Method I	Method II
RAB	20	80	99.56	98.99	0.68	1.10
		100	99.15	99.40	1.09	0.88
		120	99.28	99.24	0.72	0.73
LEV	75	80	98.25	98.92	0.21	0.313
		100	98.40	99.35	0.65	0.250
		120	98.36	99.40	0.28	0.361

Table 3 Percent recovery of rabeprazole sodium and levosulpiride in the presence of excipients.

Excipients	Amount of excipient ($\mu\text{g/ml}$)	RAB recovery		LEV recovery	
		% Amt found \pm % RSD ($n = 5$)		% Amt found \pm % RSD ($n = 5$)	
		Method I	Method II	Method I	Method II
Lactose	38.88	99.75 \pm 0.81	99.91 \pm 0.58	99.80 \pm 0.70	101.20 \pm 0.37
Lactose	50.85	99.10 \pm 0.70	99.65 \pm 0.85	100.10 \pm 0.95	100.80 \pm 0.60
Starch	1.79	100.30 \pm 0.95	100.10 \pm 0.45	99.90 \pm 0.55	99.15 \pm 0.80
Starch	14.95	99.80 \pm 0.45	99.15 \pm 0.30	99.75 \pm 0.35	99.65 \pm 0.78
Magnesium stearate	0.15	101.45 \pm 0.85	101.25 \pm 0.65	101.15 \pm 0.25	101.10 \pm 0.55
Magnesium stearate	2.99	101.25 \pm 0.25	100.30 \pm 0.45	100.45 \pm 0.65	99.55 \pm 0.30

Table 4 Application of proposed method for analysis of tablet formulation.

Drug	RAB ($n = 5$)			LEV ($n = 5$)		
	Method I	Method II	Reported method	Method I	Method II	Reported method
Label claim	20			75		
Amt found	20.09	19.89	19.89	73.81	74.73	74.30
% Amt found	100.5	99.45	99.48	98.41	99.64	99.06
% RSD	1.41	0.79	0.29	0.33	0.50	0.57
<i>t</i> -Value	1.0205	1.0512	–	0.2915	1.71	–
<i>F</i> -value	0.04155	0.1379	–	2.2367	1.2871	–

$t = 2.776$ ($n = 5$, 0.05%), $F = 6.39$ ($n = 5$).

Table 5 Dissolution parameters for rabeprazole sodium and levosulpiride.

Dissolution parameters	
Dissolution apparatus	USP apparatus II (Paddle)
Dissolution medium	Phosphate buffer pH 7.4
Volume of dissolution medium	900 ml
Speed of paddle rotation	100 rpm
Temperature	37 \pm 0.5 $^{\circ}\text{C}$
Sampling time	Up to 24 h

4.8. LOD and LOQ

The values for limit of detection and limit of quantitation by both methods are mentioned in (Table 1).

4.9. Specificity study

The recovery results indicated that the proposed methods were specific one. No interference was found from listed excipients and recovery values were 99.10-101.45% for method I and

99.15-101.20% for method II (Table 3). The result shows no excipient interference in drug analysis by both optimized spectroscopic methods.

4.10. Drug product evaluation

The marketed brand of tablet was analyzed and amount of RAB and LEV determined by the proposed method was found to be 100.5% for RAB and 98.41% for LEV, respectively by simultaneous equation method and 99.45% for RAB and 99.64% for LEV by employing first derivative spectroscopic method (Table 4).

4.11. Comparison with the reported method

The results of developed methods were compared with the reported method and expressed in terms of *t* value and *F* value (Table 4). The calculated *F* value was less than the critical value 6.39 for variance at α 0.05%. The calculated *t* value was also less than theoretical critical value 2.776 for the two optimized spectroscopic methods. The differences between means

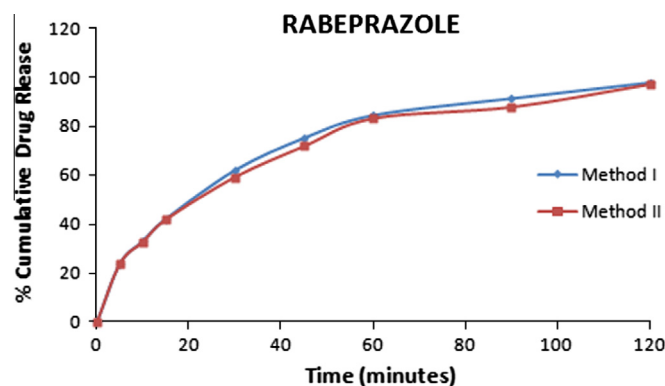


Figure 5 Dissolution profile of rabeprazole sodium employing methods I and II.

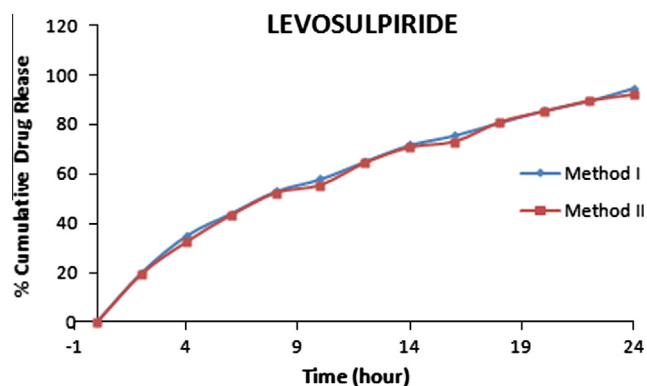


Figure 6 Dissolution profile of levosulpiride employing methods I and II.

were considered insignificant. The comparison with the reported method shows that the developed methods are accurate and precise.

4.12. Dissolution study

The dissolution conditions were optimized after evaluating the release using different dissolution media viz. 0.1 N HCl, pH 4.5 acetate buffer and pH 7.4 phosphate buffer. The release profile was also evaluated at different speed of paddle rotations i.e. at 50, 75 and 100 rpm. The optimized dissolution conditions are mentioned in (Table 5). The % cumulative drug release of RAB and LEV was evaluated by simultaneous equation method and first derivative spectroscopic method. It was found satisfactory for Rabeprazole and extended release of Levosulpiride as shown in Figs. 5 and 6.

5. Conclusion

The most noteworthy feature of this method is its simplicity and rapidity and non-requiring-time consuming sample preparations such as extraction of solvents, heating, and degassing which are needed for the HPLC procedure. These are novel methods and can be employed for routine analysis in quality control analysis. The described methods are giving accurate and precise results for the determination of Rabeprazole

Sodium and Levosulpiride mixture in marketed formulation. The proposed methods could be satisfactorily employed in dissolution studies to determine the percentage drug release.

References

- Agarwal, N., Jagdigsh, B., 2012. Development and validation of stability indicating RP-HPLC method for simultaneous estimation of levosulpiride and rabeprazole sodium. *International Journal of Pharma and Bio Sciences* 3 (4), 718–726.
- Barbeau, D.L., 2008. Sulpiride Pharmaceutical Compositions. Williamsburg Holdings LLC, US (pp. 1–10).
- Bhalodia, H.A., Boda, J.M., Patel, P.B., 2012. Application of absorbance ratio method for simultaneous spectroscopic estimation of rabeprazole sodium and levosulpiride in combined pharmaceutical formulation. *Inventi Rapid: Pharma Analysis and Quality Assurance*, 4, Article ID-“Inventi:ppaqa/320/12”, 2012 [cited 2013 Feb 04]. Available from: <<http://www.inventi.in/Article/ppaqa/320/12>>.
- Bharathi, D.V., Hotha, K.K., Jagadeesh, B., Chatki, P.K., Thriveni, K., Mullangi, R., Naidu, A., 2009. Simultaneous estimation of four proton pump inhibitors – lansoprazole, omeprazole, pantoprazole and rabeprazole: development of a novel generic HPLC-UV method and its application to clinical pharmacokinetic study. *Biomedical Chromatography* 23, 732–739.
- Brown, C.K., 2005. *Pharmaceutical Dissolution Testing*, Taylor and Francis, Group, 341–368.
- China Raju, B., Shilpa, S., Sai Annapurneswari, T., Jayathirtha rao, V., Rajesh, B., Venkateshwarao, P., 2012. Simultaneous estimation and validation of levosulpiride and rabeprazole sodium in bulk and pharmaceutical dosage form by RP-HPLC method. *Journal of Pharmaceutical Research* 5 (10), 5010–5013.
- Choudhary, B., Goyal, A., Khokra, S.L., Kaushik, D., 2009. Simultaneous estimation of diclofenac sodium and rabeprazole by high performance liquid chromatographic method in combined dosage forms. *International Journal of Pharmaceutical and Drug Research* 1, 43–45.
- Dave, H.N., Mashru, R.C., Thakkar, A.R., 2007. Simultaneous determination of salbutamol sulphate, bromhexine hydrochloride and etofylline in pharmaceutical formulations with the use of four rapid derivative spectrophotometric methods. *Analytica Chimica Acta* 597, 113–120.
- Garcia, C.V., Paim, C.S., Steppe, M., Schapoval, E.E.S., 2006. Development and validation of a dissolution test for rabeprazole sodium in coated tablets. *Journal of Pharmaceutical and Biomedical Analysis* 41, 833–837.
- Gunji, R., Nadendla, R.R., Ponnuru, V.S., 2012. Simultaneous UV-spectrophotometric determination and validation of diclofenac sodium and rabeprazole sodium using hydrotropic agents in its

- tablet dosage form. *International Journal of Drug Development and Research* 4, 316–324.
- ICH validation of analytical procedures: text and, methodology Q2 (R1), 2005.
- Indian Pharmacopoeia, 2010. sixth ed. Indian Pharmacopoeial Commission, Ghaziabad (vol. 3, pp. 2037–2038).
- Manjunath, S., Chouhan, V., Sandeep, S., 2011. Spectrophotometric estimation of levosulpiride in bulk drug and formulations. *International Journal of Pharmacy and Pharmaceutical Sciences* 3, 135–137.
- Naguib, I.A., Abdelkawy, M., 2010. Development and validation of stability indicating HPLC and HPTLC methods for determination of sulpiride and mebeverine hydrochloride in combination. *European Journal of Medicinal Chemistry* 45, 3719–3725.
- Osman, A., Osman, M., 2009. Spectrofluorometry, thin layer chromatography, and column high-performance liquid chromatography determination of rabeprazole sodium in the presence of its acidic and oxidized degradation products. *Journal of AOAC International* 92, 1373–1381.
- Patel, R. B., Patel M. R., 2008. An Introduction to Analytical Method Development for Pharmaceutical Formulations. *Pharma Review*, Volume: 6; Issue: 4;2008 [cited 2013 May 10] Available from <http://www.pharmainfo.net/reviews/introduction-analytical-method-development-pharmaceutical-formulations>.
- Patel, S.K., Desai, P.P., Raval, M.A., 2012. Development and validation of high performance liquid chromatography method for simultaneous estimation of levosulpiride and rabeprazole sodium in combined pharmaceutical formulation. *Inventi Rapid: Pharm Analysis and Quality Assurance*, Article ID-“Inventi:ppaqa/452/12”, [cited2013Feb04]. Available from: <<http://www.inventi.in/Article/ppaqa/452/12.aspx>> .
- Pekamwar, S.S., Kalyankar, T.M., Attar, M.S., 2013. Simultaneous estimation of rabeprazole sodium and levosulpiride by UV-spectrophotometry in tablet formulation. *Analytical Chemistry* 12, 15–19.
- Rahman, N., Bano, Z., Azmi, S.N.H., 2008. Quantitative analysis of rabeprazole sodium in commercial dosage forms by spectrophotometry. *Chemical and Pharmaceutical Bulletin* 56, 995–1001.
- Siewert, M., Dressman, J., Brown, C.K., Shah, V.P., Aiache, J.M., Aoyagi, N., Bashaw, D., Brown, C., Brown, W., Burgess, D., 2003. FIP/AAPS guidelines to dissolution/in vitro release testing of novel/special dosage forms. *AAPS PharmSciTech* 4, 43–52.
- Sirisha, A., Ravikumar, A., 2012. Method development and validation of simultaneous estimation of levosulpiride and rabeprazole in bulk and pharmaceutical dosage form by RP-HPLC. *International Research Journal of Pharmaceutical and Applied Sciences* 2, 49–55.
- Suganthi, A., John, S., Ravi, T.K., 2008. Simultaneous HPTLC determination of rabeprazole and itopride hydrochloride from their combined dosage form. *Indian Journal of Pharmaceutical Sciences* 70, 366.
- Swan, S.K., Hoyumpa, A.M., Merritt, G.J., 1999. Review article: the pharmacokinetics of rabeprazole in health and disease. *Alimentary Pharmacology and Therapeutics* 13, 11.
- Swartz, M., 2011. Developing and validating dissolution procedures for improved product quality. *Pharma Times* 43, 4–12.
- The Merck Index, 13th ed. Merck Research Lab, Division of Merck and Co., Inc., Whitehouse Station, NJ (pp. 8180–9080).
- Tripathi, K.D., 2003. *Essentials of Medical Pharmacology*. Jaypee Brothers Medical Publishers, New Delhi (p. 593).
- United States Pharmacopoeia and National Formulary, 2009. *United States Pharmacopoeial Convention, Inc., Rockville, MD* (p. 599).
- Walash, M.I., El-din, M.M.K.S., El-enany, N.M., Eid, M.I., Shalan, S.M., 2012. Simultaneous determination of sulpiride and mebeverine by HPLC method using fluorescence detection: application to real human plasma. *Chemistry Central Journal* 6, 13.