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Research Article

DEVELOPMENT OF FIRST ORDER DERIVATIVE ULTRAVIOLET SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF LEVOCETIRIZINE HYDROCHLORIDE AND PHENYLEPHRINE HYDROCHLORIDE IN BULK AND COMBINED DOSAGE FORM

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ABSTRACT
The first order derivative method of ultraviolet spectrometry for simultaneous determination of Levocetirizine hydrochloride (LEV) and Phenylephrine hydrochloride (PHE) in bulk drug and combined dosage form was found to be simple, accurate, fast, precise and reproducible. Methanol was used as solvent for the study. The linearity for zero order derivative method was carried out by using the concentration range 3-9 µg/ml for LEV and 6-18 µg/ml for PHE. The coefficient correlation of LEV and PHE for zero order was found to be 0.9993 and 0.9996 respectively. At zero crossing point of LEV (230nm) PHE showed a measurable derivative absorbance where as at the zero crossing point of PHE (216nm), LEV showed appreciable derivative absorbance value. Precision study showed that % RSD was within the range of acceptable limits (<2). The % recovery for LEV and PHE was found to be in the range of 98-100% and 100-102% respectively and in the marketed formulation PHE and LEV was found as 99.19% and .99.88% respectively. The developed method was validated as per ICH Q2 (R1) guidelines and results obtained with a high percentage of recovery, good accuracy and precision.
Keywords: Levocetirizine Hydrochloride, Phenylephrine hydrochloride, UV derivative spectrophotometry, first order derivative spectrophotometry.

INTRODUCTION

Levocetirizine (LEV) is [2-[4-[(R)-(4-Chlorophenyl) phenylmethyl]-1piperazinyl]ethoxy]-acetic acid dihydrochloride[1]. It is a third generation non-sedative antihistaminic agent, used in the treatment of idiopathic urticaria and allergic rhinitis[2]. Levocetirizine dihydrochloride is official in IP[3]. Phenylephrine (PHE) is chemically given as (R)-2-methylamino-1-(3-hydroxyphenyl) ethanol hydrochloride). It is a selective α1-adrenergic receptor agonist and acts as sympathomimetic agent[4]. It is official in IP[5], BP[6]. Both of these drugs are used in cold and cough preparations either individually with other drugs or in combinations.

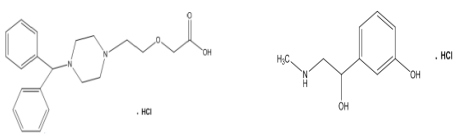

Figure 1: Chemical structures of Levocetirizine hydrochloride and Phenylephrine hydrochloride

Literature survey showed that several HPLC[7, 8, 9] and spectrophotometric[10, 11, 12] methods have been developed either alone or in combination, but no method was found for the selected combined dosage form by first order derivative UV spectophotometry. Derivative spectrophotometry[13, 14] is one of the advanced spectrophotometric techniques useful for determination of quantitative and qualitative analysis. It has a great capability to resolve the overlapping spectra in those methods which lack selectivity. The objective of this work was to develop a simple, accurate and sensitive method for determination of Levocetirizine hydrochloride and Phenylephrine hydrochloride in bulk as well as combined dosage form.

MATERIALS AND METHODS

Apparatus

A double beam JASCO UV-visible Spectrophotometer (model- V530) with a matched pair of 1cm quartz cells was used for all spectral measurements. All the spectral data was processed using software 'Spectra Manager'.

Materials

Pure drug sample of Levocetirizine hydrochloride was obtained as gift sample from FDC Pvt. Ltd, Mumbai and Phenylephrine hydrochloride was obtained from EMCURE Pvt. Ltd. Mumbai). The commercially available tablets (LAZINE D, GenX pharma) containing Phenylephrine hydrochloride 10mg and Levocetirizine hydrochloride 5mg was purchased from local market.

Method Development

Preparation of standard stock solution

The stock solutions having 1mg/ml concentration of LEV and PHE were prepared separately by dissolving accurately weighed quantities of both drugs in methanol. Further dilutions of the standard stock solutions of both drugs were made with methanol to get the working standard solution of 100µg/ml concentration.

Selection of scanning range and sampling wavelength

The standard solutions of LEV and PHE were diluted with methanol individually to get the concentration of 5µg/ml and 10µg/ml respectively and were scanned in the UV range 400-200nm. The λmax of both the drugs were found to be 230nm and 216 nm respectively. The spectral data was processed to obtain first order derivative spectrum at wavelength interval of 2 nm and scaling factor 10 for the range of 400-200nm with scanning speed of 400nm/min. It was observed that LEV shows zero crossing at 230nm while PHE shows zero crossing at 216nm. At zero crossing point of LEV (230nm), PHE showed a measurable dA/dλ whereas at zero crossing

point of PHE (216nm), LEV showed a measurable dA/dλ. Hence the wavelengths 230nm and 216nm were selected as analytical wavelengths for determination of LEV and PHE first order derivative method respectively.

Method Validation

The above proposed method was validated according to International conference on harmonisation Q2 R1 (ICH Q2R1) guidelines[15] for validation of analytical procedures in order to determine the linearity, Accuracy, Precision, and assay of market formulation.

Linearity

For linearity studies, aliquots of drug solutions were further diluted with methanol to get the final working standard solution. The linearity was evaluated by the regression analysis. The corresponding regression equation was found to be for

Levocetirizine: $y = 0.0529x + 0.0467$, $R^2 = 0.9993$
Phenylephrine: $y = 0.0316x + 0.1764$, $R^2 = 0.9996$

Accuracy

To assess accuracy of the method, recovery studies were carried out by the standard addition method. For this, known quantities of pure LEV and PHE equivalent to 80, 100, and 120% of their label claim in commercial tablets were mixed with corresponding definite amounts of pre-analysed formulations such that final concentrations of the drugs were within the linearity range. The total amount of each drug was then determined and the drug added amount was calculated.

Precision

The precision was determined with standard samples of both drugs prepared in triplicates at three different concentration levels covering the entire linearity range. The precision was calculated by intraday and interday and reported as % RSD.

Assay of Marketed Formulation

Ten tablets were weighed and powder equivalent to 10mg of PHE and 5mg of LEV was weighed and transferred to 100ml volumetric flask, volume adjusted with methanol.1.5 ml of this standard solution was pipette out and diluted to 10ml with methanol to get the solution containing 10µg/ml PHE and 5µg/ml LEV. Absorption spectra of the prepared solution were recorded and concentration of each drug was calculated using calibration curve equation.

Calibration Curves for First Order Derivative

The aliquots of both the drugs used in linearity studies were converted to first derivative spectra and the derivative absorbance at 230nm and 216nm for PHE and LEV were measured respectively. The calibration graphs of both drugs were plotted at 230nm 216 nm. The following regression equations for both the drugs were obtained as:

Levocetirizine: $y = 0.0031x + 0.0004$, $R^2 = 0.9993$
Phenylephrine: $y = 0.0018x + 0.0126$, $R^2 = 0.9984$

Table 1: Results showing linearity of LEV and PHE

Sr. No.	Conc. Of drug (µg/ml) (LEV)	Absorbance by zero order	Conc. Of drug (µg/ml) (PHE)	Absorbance by zero order
1	3	0.2083	6	0.368
2	4	0.25438	8	0.43192
3	5	0.31352	10	0.48997
4	6	0.36349	12	0.55279
5	7	0.41218	14	0.61589
6	8	0.47055	16	0.68481
7	9	0.52462	18	0.74764
Regression equation	y = 0.0529x + 0.0467		y = 0.0316x + 0.1764	
Correlation coefficient	0.9993		0.9996	
Slope	0.0529		0.0316	
Intercept	0.0467		0.1764	

Table 2: Results of Recovery studies

Drug	Conc. Of std. drug	Recovery level	Amt. of drug added	Total amount of drug	% recovery (n=3)
LEV	4ug	80%	3.2	7.2	102.81
		100%	4	8	100.2
		120%	4.8	8.8	101.98
PHE	8ug	80%	6.4	14.4	98.75
		100%	8	16	99.10
		120%	9.6	17.6	100.67

Table 3: Results of precision studies

Drug	Conc of drug (ug/ml)	%RSD*(n=3)	
		Intraday	Interday
PHE	8	0.431333	0.4300
	12	0.552097	0.5516
	16	0.684403	0.684567
LEV	4	0.259683	0.259137
	6	0.363607	0.363863
	8	0.46325	0.460323

*%RSD: % Relative standard deviation

Table 4: Result of assay of marketed formulation

Drug	Label claim (mg)	Amount found(mg)	% assay	% RSD*
LEV	5	4.994	99.88	0.65344
PHE	10	9.919	99.19	0.71514

*%RSD: % Relative standard deviation

Table 5: Results of first order derivative linearity of LEV and PHE

Sr. No.	Conc. Of drug LEV (µg/ml)	Absorbance by first order derivative	Conc. Of drug PHE (µg/ml)	Absorbance by first order derivative
1	3	0.009525	6	0.023436
2	4	0.012645	8	0.026844
3	5	0.016179	10	0.030541
4	6	0.018826	12	0.033519
5	7	0.021812	14	0.037067
6	8	0.024943	16	0.040946
7	9	0.028131	18	0.045003
Regression equation	y = 0.0031x + 0.0004		y = 0.0018x + 0.0126	
Correlation coefficient	0.9993		0.9984	
Slope	0.0031		0.00018	
Intercept	0.0004		0.0126	

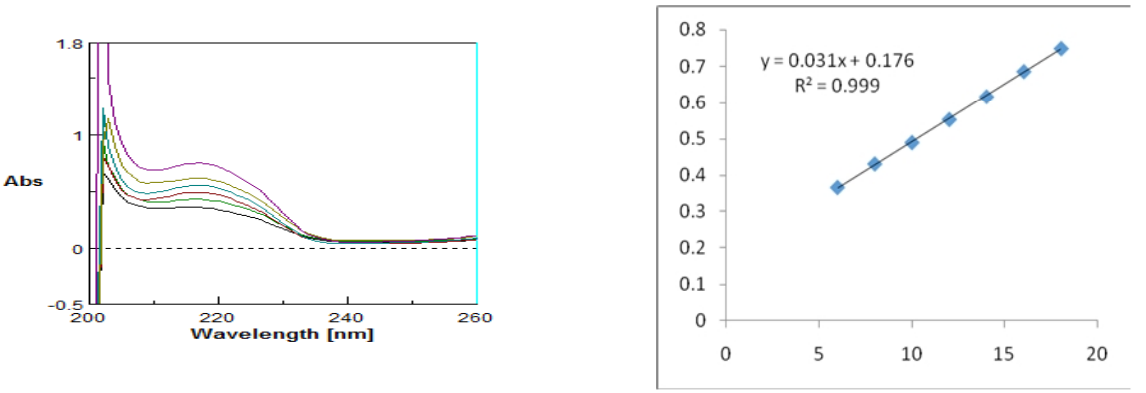

Figure 2: Linearity graph for zero order of LEV (3-9µg/ml)

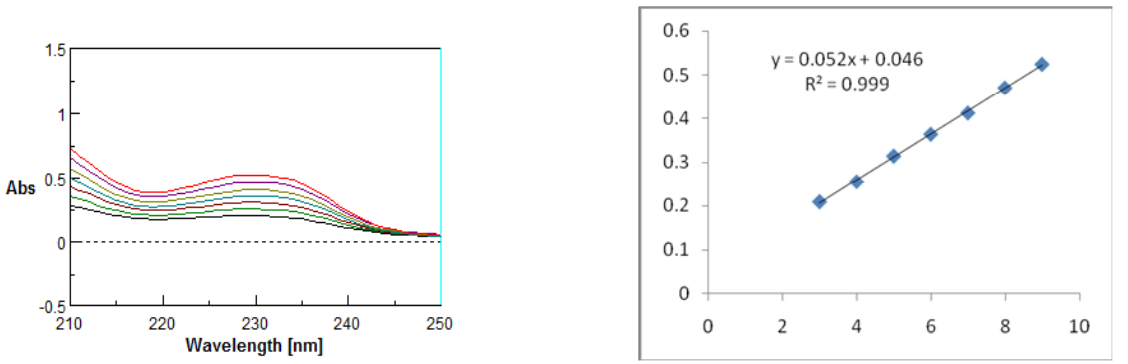

Figure 3: Linearity graph for zero order of PHE (6-18µg/ml)

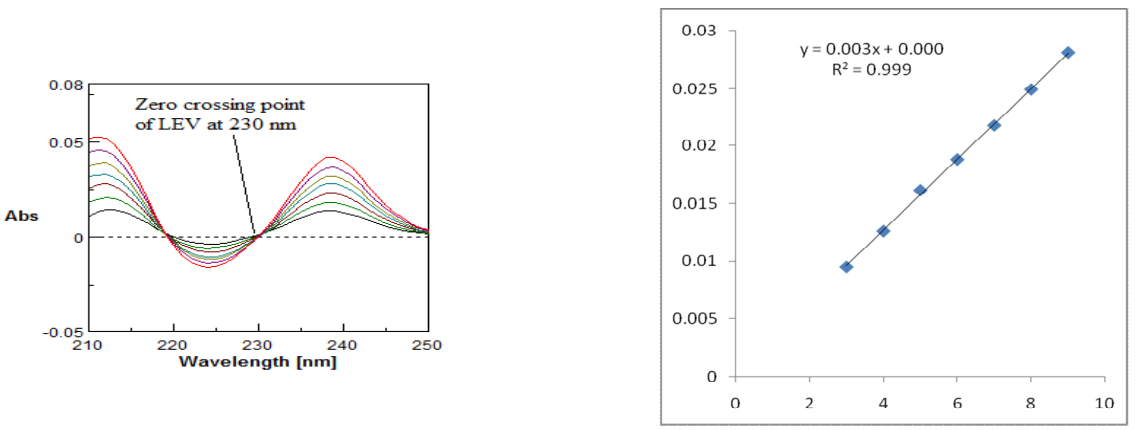

Figure 4: Linearity graph for first order of LEV (3-9µg/ml)

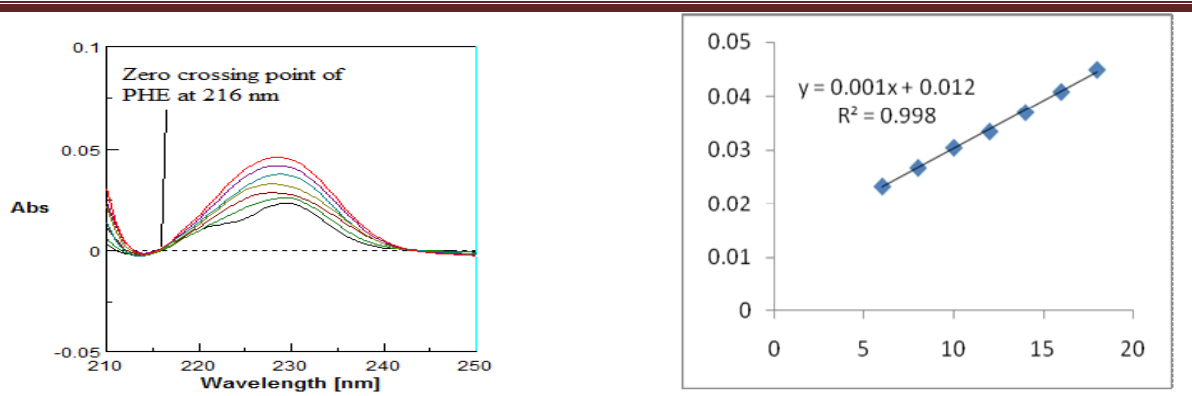

Figure 5: Linearity graph for first order of PHE (6-18µg/ml)

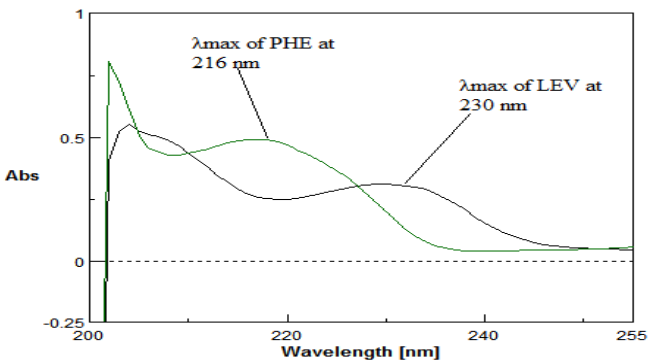

Figure 6: Overlapped spectra of LEV (5µg/ml) and PHE (10µg/ml)

RESULT AND DISCUSSION

From experimental condition described, linearity, Accuracy, Precision and assay of marketed formulation were performed. Results of linearity for zero order and first order derivative are shown in Table 1. Both the drugs obey Beer's law in the concentration range of 3-9 µg/ml for LEV and 6-18 µg/ml for PHE for zero order and first order derivative method. Result of recovery studies are shown in Table 2. The recovery study done by standard addition method has given satisfactory results as LEV 98-100% and PHE 100-102% at three concentration levels. Precision study showed that % RSD was within the range of acceptable limits (<2), as shown in Table 3. The % assay in the marketed formulation PHE and LEV was found as 99.19% and .99.88% respectively. Results of assay are shown in Table 4. Results of linearity for first order derivative are shown in Table 5.Both the drugs LEV and PHE were found to be linear over the concentration range 3-9µg/ml and 6-18µg/ml respectively in first order derivative spectrophotometry method.

CONCLUSION

A fast, simple, accurate method was developed for the estimation of LEV and PHE in combination using first order derivative UV spectrophotometric technique. The developed method can be successfully applied to analysis of marketed formulation.

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