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Development of Spectrophotometric method for the Simultaneous estimation of Phenylephrine and Levocetirizine in Pharmaceutical dosage

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Abstract:
A simple, accurate, rapid and precise spectrophotometric method has been developed for the simultaneous estimation of Phenylephrine and Levocetirizine in pharmaceutical dosage form. The method is based on UV spectrophotometric determination of two drugs, using Area under
Curve method. It involves measurement of area under curve in the range of 271-281 nm for Phenylephrine and 225-235nm for Levocetirizine. The linearity was observed in the concentration range of 2-10µg/ml for Phenylephrine and Levocetirizine. The accuracy of the method was assessed by recovery studies and was found to be 98.90 % and 98.0% for Phenylephrine and Levocetirizine respectively. The method showed good reproducibility and recovery with % RSD less than2. The method was found to be rapid, specific, precise and accurate and can be successfully applied for the routine analysis of Phenylephrine and Levocetirizine in bulk and combined dosage form without any interference from the excipients. The method was validated according to ICH guidelines and was found to be satisfactory.

Keywords: Phenylephrine, Levocetirizine,Area Under Curve, Validation, Tablets

1. Introduction

Phenylephrine (PHE) is *m*-Hydroxyphenyl-2-methylamino-ethanol (Figure 1). It is a a-adrenergic agonist most commonly used either topically or orally for symptomatic relief of nasal congestion. It is used as decongestant in treatment of fecal incontinence. In ophthalmology it is used as mydriatic[1,2]. Levocetirizine (LEV) (Figure 2) is chemically (2-(4-((4-Chlorophenyl)-phenylmethyl)-1-piperazinyl) ethoxy) acetic acid. It is a non-sedating type histamine H1-receptor antagonist used for symptomatic relief of allergic conditions including rhinitis and chronic urticaria[3,4]. Literature survey reveals that only spectrophotometric methods[5-7] and RP-HPLC methods[8-10] have been reported for the simultaneous estimation of PHE and LEV. The present work reports the development and validation of a precise and accurate Area Under Curve method for the simultaneous determination of PHE and LEV in tablet formulation. The proposed method is validated as per ICH guidelines [11].

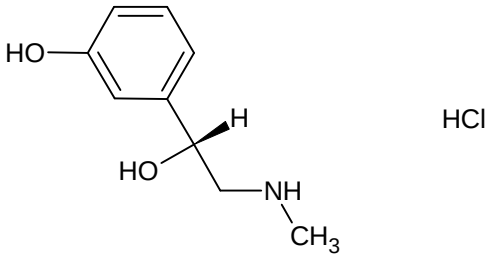

Fig 1: Structure of Phenylephrine

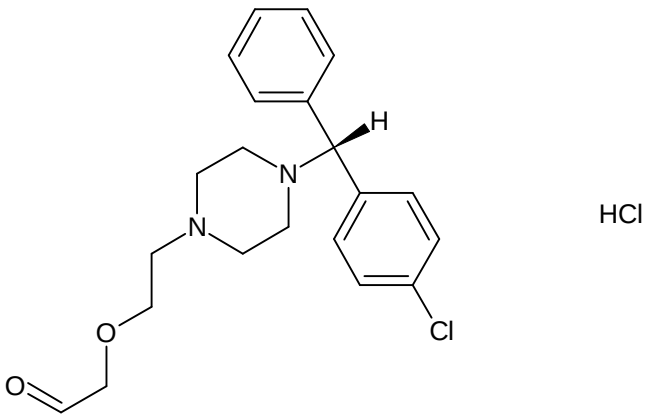

Figure 2: Structure of Levocetirizine

Instrumentation:

SHIMADZU double beam UV visible spectrophotometer (model 1800) with 1 cm matched quartz cells were used for all absorbance measurements. Shimadzu AUX 220 balance was used for weighing the samples. All statistical calculations were carried out using Microsoft Excel 2007 analytical tool.

Reagents:

Working Standards of pharmaceutical grade PHE and LEV were obtained as gift samples from M/s Centaur Pharmaceuticals, Pune and Emcure Pharmaceuticals, Pune. The tablet Lazine D was procured from the local pharmacy. All the chemicals and reagents used were of AR grade obtained from M/s Merck Ltd., Mumbai, India.

Preparation of standard solution

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

Selection of scanning range and sampling wavelength

4 µg/ml solution were prepared from working standard solution for both drugs and were scanned in the UV range 400-200nm. The wavelength maxima for LEV and PHE were found to be 230 nm and 276 nm respectively. Area under curve in the range of 225-235 nm and 271-281 nm was measured for the analysis of LEV and PHE respectively.

Preparation of Calibration curve of PHE and LEV

The standard stock solution (100 µg/ml) of PHE and LEV were further diluted to obtain the final concentration of 2-10 µg/ml for both PHE and LEV. Both the solutions were scanned in the spectrum mode from 200.0nm to 400.0nm. The maximum absorbance of PHE and LEV was observed at 276 nm and 230nm, respectively. From the overlain spectra of both drugs obtained after scanning of standard solution of PHE and LEV, area under the curve in the range of 271-281 nm (Figure 3) and225-235 nm (Figure 4)was measured for the analysis respectively. The absorptivity values were calculated. The calibration curve was plotted with concentration versus area under the curve and regression equation was calculated.

Determination of Absorptivity values:

Absorptivity = Absorbance/ Concentration of that component in gm/l.

Concentration of LEV and PHE was calculated using the following formula:

$C_{LEVO} = A_2ay1 - A_1ay2 / ax2ay1 - ax1ay2$ (1)

$C_{PHENYL} = A_1ax2 - A_2ax1 / ax2ay1 - ax1ay2$ (2)

Where,

C_{LEV} = Concentrations of LEV,

C_{PHE} = Concentrations of PHE,

A1 = Area at 225-235 nm,

A2 = Area at 271-281 nm,

ax1 = Absorptivity value of LEV at 225-235 nm,

ax2 = Absorptivity value of LEV at 271-281 nm,

ay1 = Absorptivity value of PHE at 225-235 nm,

ay2 = Absorptivity value of PHE at 271- 281nm.

Assay of marketed formulation:

Twenty tablets of brand lazine D (GenXpharma) containing 5mg of LEV and 10 mg of PHE were weighed, average weight determined and finely powdered. Appropriate quantity of powder equivalent to 5 mg of LEV and 10 mg of PHE was accurately weighed, transferred to a 100 ml volumetric flask and volume was made up to 100 ml with methanol and shaken for 15 min. It was then filtered through wharman filter paper and necessary dilution of filtrate was made with methanol to get final concentration of 5 µg/ml of LEV and 10 µg/ml of PHE. Area under curve in the range of 225-235 nm and 271-281 nm was measured for the analysis of LEV and PHE respectively. By using the calibration curve, the concentration of the sample solution was determined. The optical and statistical parameters are shown in Table 1 and the results of market sample analysis are shown in Table 2.

Method validation

Linearity

For the linearity studies, from the working standard solution, further dilutions were made to get concentration of both drugs in the range of 2µg/ml to 10 µg/ml. The calibration curve of Area under curve against concentration was plotted. Correlation coefficient and regression line equations for LEV and PHE were 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 studies and reported as % RSD as shown in Table 3.

Accuracy

To study the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels. A known amount of drug was added to pre-analyzed tablet powder and percentage recoveries were calculated.

Specificity

The specificity of an analytical method is ability to measure accurately an analyte in presence of interferences like synthetic precursor, excipients, degradants, or matrix component. The proposed derivative spectrophotometric method is able to assess the analyte in presence of excipients, and, hence, it can be considered specific.

Table 1: Optical and Statistical parameters

Parameters	FEB	DIC
Absorption maximum/ Wavelength range(nm)	200-400	200-400
Linearity Range(µg/mL)	2-10	2-10
Correlation coefficient	0.9985	0.999
Standard Error(SE)	0.0424	0.0122
Regression Equation y=mx+c	0.021x + 0.034	0.029x + 0.013
Intercept (c)	0.034	0.013
Slope (m)	0.021	0.029
LOD(µg/mL)	0.1180	0.1212
LOQ(µg/mL)	0.3601	0.3672

Table 2: Assay and recovery of PHE and LEV

Method	Labelled amount (mg)	Amount obtained (mg)*	Percentage recovery*
PHE	10	9.89	98.90
LEV	5	4.90	98.00

*Average of six determinations

Table 3: Precision study

Drug	Conc. of drug(µg/ml)	% RSD	
		Intraday	Interday
PHE	4	0.454440	0.236091
	6	0.729200	0.413209
	8	0.745303	0.272537
LEV	4	1.112578	0.497813
	6	0.408378	0.439648
	8	0.402111	0.561149

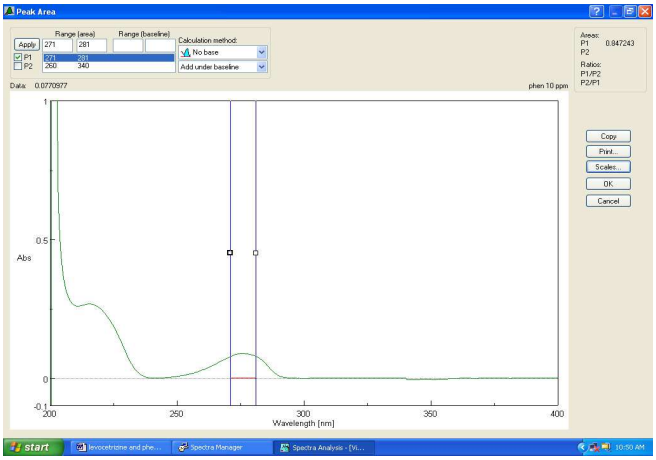

Figure 3: AUC of PHE

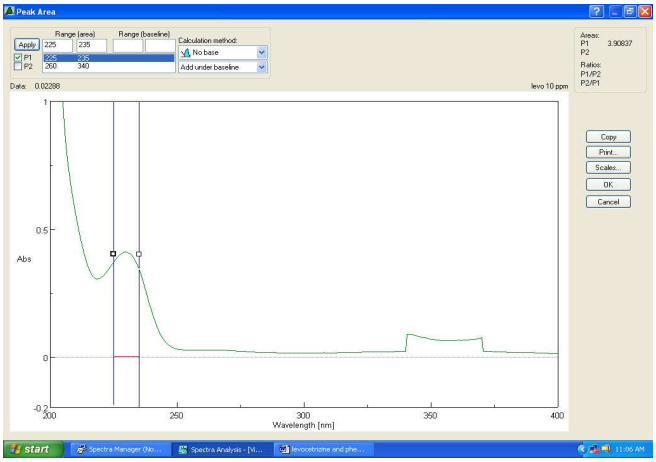

Figure 4: AUC of LEV

Results and Discussion

The present work provides an accurate, reproducible and sensitive method for the simultaneous analysis of PHE and LEV in its bulk and pharmaceutical dosage form. Area under curve in the range of 225-235 nm and 271-281 nm was measured for the analysis of LEV and PHE respectively. Linearity for detector response was observed in the concentration range of 2-10µg/ml for and LEV. Standard deviation and coefficient of variance for six determinations of tablet formulation, was found to be less than ± 2.0 indicating the precision of the methods. Accuracy of proposed methods was ascertained by recovery studies and the results are expressed as percentage recovery. Values of standard deviation and coefficient of variation was satisfactorily low indicating the accuracy of all the methods. % RSD for Intraday assay precision for PHE and LEV was found to be 0.642 and 0.640andInterdayassay precision for PHE and LEV was found to be 0.307 and 0.499respectively. Based on the results obtained, it is found that the proposed method is accurate, precise, reproducible & economical and can be employed for routine quality control of PHE and LEV in bulk drug and its pharmaceutical dosage form.

Conclusion

UV spectrophotometric method for PHE and LEV was developed separately in bulk and tablet dosage form by Area under curve method. The method was validated as per ICH guidelines. The standard deviation and % RSD calculated for the method is<2, indicating high degree of precision of the methods. The results of the recovery studies showed the high degree of accuracy of the method. In conclusion, the developed method is accurate, precise and selective and can be employed successfully for the estimation of PHE and LEV in bulk and pharmaceutical dosage form.

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