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SIMULTANEOUS SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF LEVOCETIRIZINE AND PSEUDOEPHEDRINE IN PHARMACEUTICAL TABLET DOSAGE FORM.

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ABSTRACT
Two methods for simultaneous estimation of Levocetirizine dihydrochloride (LEVC) and Pseudoephedrine hydrochloride (PSEUDO) in two component solid dosage forms have been developed. The methods employ the application of simultaneous equation and the absorbance ratio (Q-analysis) method. All these methods utilize distilled water as a solvent. LEVC shows maximum absorbance at a wavelength of 231 nm and PSEUDO at 257 nm, where the linearity ranges for LEVC and PSEUDO were 5-30 µg/ml and 120-960 µg/ml, respectively. Determination of ratio of absorbance at 231 nm (the maximum absorption of LEVC) and isobestic wavelength 242 nm, the linearity ranges for LEVC and PSEUDO were 5- 30 µg / ml and 120-960 µg / ml, respectively. The procedures were successfully applied for the simultaneous determination of both the drugs in laboratory prepared mixtures and in commercial tablet preparation. The accuracy of the methods was assessed by recovery studies and was found to be ranging from 97.87-99.70% for LEVC and 99.01-99.79% for PSEUDO by the simultaneous equation method, 98.99-101.42% for LEVC and 99.57-99.91% for PSEUDO by the graphical absorbance ratio method.

KEYWORDS: Combined tablet dosage form, Levocetirizine dihydrochloride, Pseudoephedrine hydrochloride, Simultaneous estimation.

INTRODUCTION

The Levocetirizine dihydrochloride (LEVC) is chemically (R)-2-(2-(4-((4-chlorophenyl) phenyl methyl) piperazin-1-yl) ethoxy) acetic acid is a selective potent H1-antihistamine compound indicated for the treatment of allergic rhinitis and chronic idiopathic urticaria[1] and is official in Indian Pharmacopoeia 2007.[2] Different spectrophotometric[3], HPLC[4 -7] and LC-MS[8,9]methods have been reported for the determination of cetirizine in pharmaceutical formulations and biological fluids.

Pseudoephedrine hydrochloride, is chemically (1S,2S) -2- methylamino -1-phenylpropan-1-ol hydrochloride, has sympathomimetic activity[10] and is official in the United States Pharmacopoeia[11], British Pharmacopoeia[12] and Indian Pharmacopoeia[2].All the three pharmacopoeia describe HPLC method for estimation of pseudoephedrine hydrochloride from tablet formulation. Several HPLC methods [13, 16] and few LC/MS methods [17, 18] are reported for the estimation of pseudoephedrine hydrochloride. Both the drugs are formulated in a binary solid dosage form for the treatment of allergic conditions like allergic rhinitis, cough and cold for relief of nasal decongestion. Literature survey revealed that single HPLC [18] method has been reported for the simultaneous estimation of both these components in a combined dosage form. But no spectrophotometric method has been reported for estimation of this combination. The aim of this paper was to develop the simultaneous equation (Vierodt's) method, the absorbance ratio (Q-analysis) method for estimating LEVC and PSEUDO simultaneously in their mixture form. In the

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proposed methods no separation is required; the methods are fast and convenient.

MATERIALS AND METHODS

Instrument, reagents and chemicals

A dual-beam Shimadzu UV-visible spectrophotometer 1700 Pharmaspec was used. Freshly prepared distilled water was used as a solvent. Gift samples of LEVC and PSEUDO were procured from FDC Pvt. Ltd.Goa and Glen mark Pvt.Ltd. Nashik respectively.

Spectral and linearity characteristics of levc and pseudo

Standard stock (100 µg/ ml) of LEVC and (1000 µg/ ml) of PSEUDO were prepared in distilled water. The aliquot portions (0.5, 0.75, 1, 1.25, 1.5, 1.75 , 2, 2.25, 2.5, 2.75, 3) from the 100 µg/ ml LEVC and (1.2, 1.8, 2.4, 3, 3.6 ,4.2, 4.8, 5.4, 6, 6.6, 7.2, 9.6) from the 1000 µg/ml working PSEUDO solutions were accurately transferred to 10-ml volumetric flasks, the volume was completed with distilled water The absorption spectra between 200- 400 nm of all solutions of LEVC and PSEUDO were measured at 231 nm (λ□max for LEVC), 257 nm (λmax for PSEUDO), 242nm (isobestic wavelength).

Application of the proposed procedures for the determination of levc and pseudo in tablets

The average weight quantity (0.5168 gm) of twenty tablets (Levocet-D, Hetero Drugs Ltd., Content- Levocetirizine 5 mg and pseudoephedrine 120 mg) was transferred to

100 ml volumetric flask and dissolved in distilled water by intermittent shaking and volume was made up to 100 ml with the same solvent. The solution was then filtered through a Whatmann filter paper (No. 41). The solution was diluted with distilled water to obtain 5 µg/ml of LEVC and 120 µg/ml of PSEUDO

This sample was scanned over the range of 200nm to 400nm in spectrum mode for the estimation of both these drugs by using simultaneous equation and absorbance ratio method (table-I). The analysis procedure was repeated six times. The selectivity of the proposed procedures was examined by determining the recovery of the two drugs by standard addition method (table-II).

RESULTS AND DISCUSSION

Simultaneous equations method [19]

The absorptivity values of the drugs were determined at the λ max of LEVC and PSEUDO respectively.The absorptivity value of the drugs is the ratio of absorbance at selected wavelengths with concentration of drugs in µg/ml. A set of two simultaneous equations were framed using these

Table I: - Result of tablet assay for content of levc and pseudo by using the proposed methods

	Simultaneous equation method		Graphical absorbance ratio method	
	Recovery(%) ± S.D.(n=6)		Recovery(%) ± S.D.(n=6)	
	LEVC	PSEUDO	LEVC	PSEUDO
Tablet	100.03 + 0.5746	100.31 + 0.5407	101.81 + 0.9502	100.04+ 0.7612
RSD (%)	0.5744	0.5389	0.9333	0.7609

S.D.: Standard deviation, RSD: Relative Standard Deviation

Table II: - Result of recovery study for the simultaneous estimation of levc and pseudo in tablet by using the proposed methods. (n=6)

Level of % recovery	Recovery of added standard (%) ±S.D.			
	LEVC		PSEUDO	
	SEM	GRM	SEM	GRM
80	97.87+ 0.615	101.42 +0.00149	99.01 +0.255	99.91 +0.00176
100	99.70 ±0.150	99.43 ±0.00131	99.69 ±0.025	99.57 ±0.00246
120	98.58 ±0.503	98.99±0.00395	99.79 ±0.129	99.75 ±0.00094
% Mean recovery	98.72+ 0.4226	99.95+ 0.00225	99.50+ 0.1363	99.74+ 0.00172

SEM- *Simultaneous equation method*
GRM-*Graphical absorbance ratio method*

absorptivity values.

$A_1 = 3443C_1 + 14C_2$ ---------- (at - 231)

$A_2 = 167C_1 + 104\ C_2$---------- (at - 257)

Where, A_1 and A_2 are absorbance values of the sample solution at 231nm and 257 nm respectively. 3443 and 167 are absorptivities of LEVC at 231 nm and257 nm, respectively. 14 and 104 are the absorptivities of PSEUDO at 231 nm and 257 nm, respectively. C_1 is the concentration of the LEVC and C_2 is the concentration of the PSEUDO in µg/ml.

The graphical absorption ratio method (Q- analysis) [19]

In quantitative assay of two components by Q-analysis method, absorbances were measured at the isobestic wavelength and maximum absorption of one of the two components. From overlain spectra of LEVC and PSEUDO shown in figure (Fig.1), absorbances were measured at the selected wavelengths i.e. 242 nm (isobestic wavelength) and 231nm (wavelength of maximum absorption of LEVC).

From the following sets of equations, the concentration of each component in sample solution can be calculated.

Concentration of LEVC = $(Q_M - 0.402299)$ $A / 3.2532*ax_1$

Concentration of PSEUDO = $(3.6554- Q_M)$ $A / 3.2532*ay_1$

Where, A = Absorbance value of sample solution at isobestic wavelength 242 nm. Q_M = Ratio of absorbance of sample solution at 231 nm to absorbance of sample solution at isobestic wavelength 242 nm. ax_1= absorptivity of LEVC at 242nm. (isobestic wavelength)

ay_1= absorptivity of PSEUDO at 242nm (isobestic wavelength)

Table III: - Data for calibration graph (n=6) for levo and onz using simultaneous equation method, absorbance ratio method,area under curve method.

Parameters	Simultaneous equation method	Absorbance ratio method
Levocetirizine		
Slope(m)	0.03327	0.009488
Intercept(c)	0.01622	0.00084
Correlation coefficient	0.9992	0.9994
Beer's law limit(µg/ml)	5-30	5-30
LOD (µg/ ml)	2.7335	2.7
LOQ (µg/ ml)	8.2833	8.28
Pseudoephedrine		
Slope	0.00964	0.00367
Intercept	0.02609	0.00299
Correlation coefficient	0.9991	0.9993
Beer's law limit(µg/ml)	120-960	120-960
LOD(µg/ ml)	81.56	65.78
LOQ(µg/ ml)	247.15	199.33

Method validation [20]

The methods were validated with respects to linearity, limit of detection (LOD), limit of quantification (LOQ), precision, accuracy and sensitivity. The results obtained are summarized in table-II, table-III and IV, respectively.

Table IV: - Precision of spectrophotometric methods developed for analysis of tablet (n=6)

	Simultaneous equation method	Absorbance ratio method
Levocetirizine		
Intra day		
Amount found(mean %+S.D)	100.03+ 0.0055	101.82 + 0.0034
Precision, RSD (%)	1.5433	0.9220
Inter day		
Amount found(mean %±S.D)	99.65 ± 0.0016	99.77 ± 0.0029
Precision, RSD (%)	0.4329	0.7979
Pseudoephedrine		
Intra day		
Amount found(mean %+S.D)	100.31 + 0.0031	100.04 + 0.0022
Precision, RSD (%)	1.2728	1.2880
Inter day		
Amount found(mean %±S.D)	99.8 ± 0.0015	99.45 ± 0.0025
Precision, RSD (%)	0.6119	1.4343

CONCLUSION

The proposed methods were found to be simple, accurate, economical and rapid for routine simultaneous estimation of two drugs. All the methods were found to be economical, as they require only distilled water as a solvent. The results obtained for tablet analysis and recovery study are summarized in table I, and II respectively. The results of validation parameters are shown in table III and IV are of satisfactory level indicates the accuracy of proposed methods for estimation of LEVC and PSEUDO. These methods can also give excellent results and can be employed for the routine analysis of these two drugs in combined dosage form.

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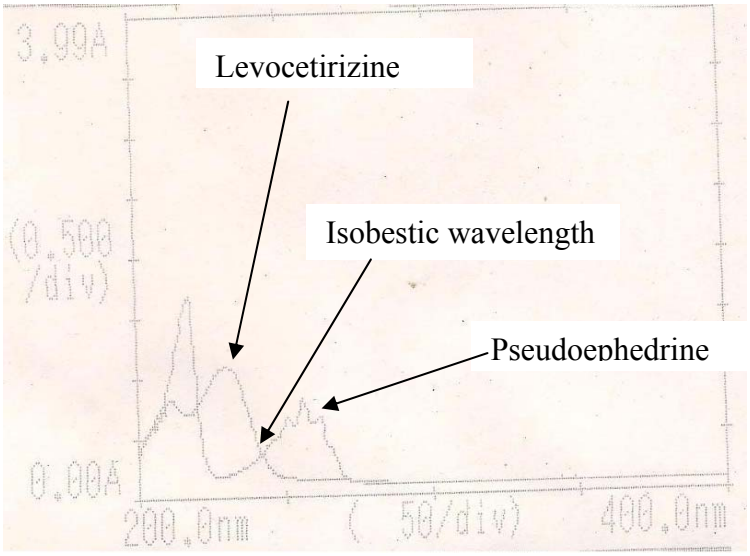

Fig.1. UV overlain spectra of levocetirizine and pseudoephedrine

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