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Concurrent Spectrophotometric Assay of Pseudoephedrine and Cetrizine from Combination Tablets

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Two simple methods based on simultaneous equations (Vierdot's Method) and absorbance difference with correlation regression equations, respectively for simultaneous estimation of pseudoephedrine and cetrizine in multicomponent formulations have been presented. Proper selection of wavelengths with utilization of correlative regression equation s and simultaneous equations eliminates complex interference raised in estimation of one drug by another. The results of analysis have been validated statistically at a 95 per cent confidence level with Student's t-test and by recovery studies.

Key Words: Spectrophotometric assay, Pseudoephedrine, Cetrizine.

INTRODUCTION

Pseudoephedrine hydrochloride (PSD) is a sympathomimetic agent primarily used as nasal decongestant in patients with allergic or vasomotor rhinitis with upper respiratory tract infections[1]. Cetrizine hydrochloride (CTZ) is an antihistaminic drug used in allergic and vasomotor rhinitis[2]. Combination tablets containing 120 mg of PSD and 5 mg CTZ are often used for symptomatic relief from perennial and seasonal vasomotor rhinitis, common cold, sinusitis and otitis[3].

Official methods for quantitative estimation of PSD in various formulations include non-aqueous titration (IP, BP)[4, 5] and HPLC (USP)[6] methods. CTZ is not official in any pharmacopoeia. A number of reported methods specify analysis of these drugs in individual or other multicomponent formulations or biological samples. The combined dosage forms of PSD and CTZ are non-official and only one reported method based on HPTLC specifies their simultaneous analysis[7]. The paper presents two simple, accurate, reproducible and economical methods for simultaneous estimation of both drugs in multicomponent fornulations. The first method is based on simultaneous equations (Vierdot's Method) whereas the second utilizes absorbance difference with correlation regression equation for quantification.

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EXPERIMENTAL

A Thermo Spectronic Genesys-2 split-beam, dual detector UV-Vis recording spectrophotometer with spectral band width of 2 nm was employed for all spectroscopic measurements using a pair of 10 mm matched quartz cells. PSD (IP), CTZ, hydrochloric acid AR and double distilled water were used throughout in the present investigation.

Standard stock solutions of both drugs were prepared separately in 0.1 N HCl and suitably diluted to different concentrations. The linearity was studied at respective absorbance maxima, *i.e.*, 257 and 231 nm respectively by least squares method. Beer's law holds good in the range 0–1200 μg/mL for PSD and 0–50 μg/mL for CTZ.

Method I: The method is based on Vierdot's method and utilizes corresponding absorbance maxima, *i.e.*, 257 nm and 231 nm respectively for quantification. The mean absorptivity coefficients of both drugs at each wavelength were determined from different dilutions (five independent determinations) of corresponding drugs within Beer's law cone range limit. Using these, sets of two simultaneous equations were framed.

$$A_{231} = 0.16C_{PSD} + 35.7C_{CTZ} \quad (1)$$

$$A_{257} = 0.916C_{PSD} + 1.869C_{CTZ} \quad (2)$$

where A_{231} and A_{257} are absorbances of samples containing PSD and CTZ at 231 and 257 nm respectively. C_{PSD} and C_{CTZ} are concentrations of PSD and CTZ in g/L. Solving both equations, the concentrations of PSD and CTZ can be readily found out.

Method II: PSD shows valley at absorbance maxima of CTZ, *i.e.*, 231 nm and shows absorbance of same magnitude at 270 nm (Fig. 1). CTZ was quantified

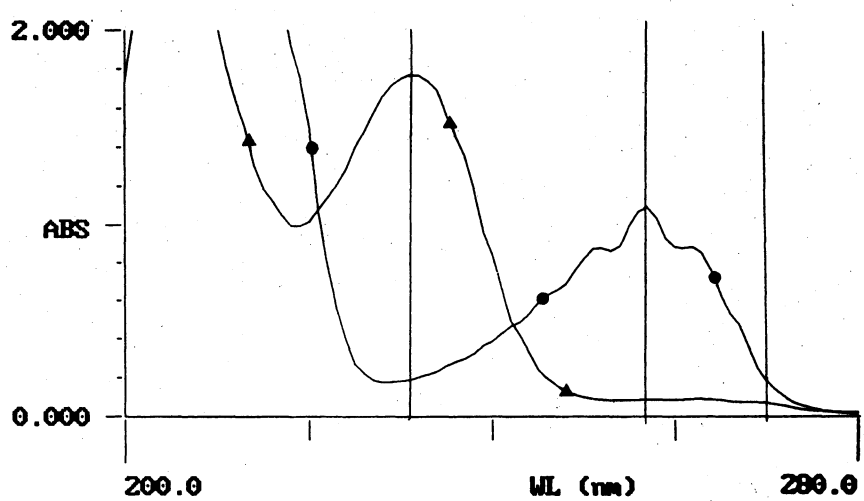

Fig. 1. Overlain spectra of PSD (•) and CTZ (▲)
*Markers showing the selected wavelengths

from the absorbance difference between 231 and 270 nm. For quantification of PSD the corresponding peak at 257 nm was selected. Although CTZ shows some interference at this wavelength, the corresponding value (A_{257}^{CTZ}) can be calculated from absorbance difference value between 231nm and 270 nm through eqn. (3). This is a linear regression equation generated from different dilutions of samples containing CTZ.

$$A_{257}^{CTZ} = 0.0548 \times (A_{231} - A_{270}) - 0.0019 \quad (n = 6, r = 0.993) \qquad (3)$$

Hence utilizing equation (3), the corresponding interference due to CTZ at 257 nm can be calculated.

For CTZ absorbance differences between 231 and 270 nm and for PSD absorbance at 257 nm were recorded from different dilutions of individual drugs. Working calibration curves were plotted with linearity validation by least squares method. Hence the final equations for quantification in samples containing both drugs are:

$$C_{CTZ} = 29.759 \times (A_{231} - A_{270}) - 0.2854 \quad (n = 5, r = 0.9997) \qquad (4)$$

$$C_{PSD} = 1096.7 \times (A_{257} - A_{257}^{CTZ}) + 0.0894 \quad (n = 5, r = 0.9999) \qquad (5)$$

Preparation of Tablet Sample Solutions: Twenty tablets were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 120 mg of PSD was transferred to a 100 mL volumetric flask. The powder was dissolved in water and the volume was made up with 0.1 N HCI. The solution was then filtered through Whatman filter paper no. 41 and labelled to contain 1200 μg/mL of PSD and 50 μg/mL of CTZ. The filtrate was suitably diluted and the absorbances at specified wavelengths were recorded. The concentrations of both drugs were worked out utilizing both the methods (Table-1).

TABLE-1
ANALYSIS OF AUTHENTIC SAMPLES (AS), RECOVERY STUDIES AND COMMERCIAL FORMULATIONS (BATCH I AND II)

	Analyte	Method-I		Method-II	
		CI	SD	CI	SD
AS	PSD	99.236 ± 1.422	1.146	100.01 ± 1.592	1.001
(n = 7)	CTZ	101.530 ± 1.804	1.134	99.59 ± 1.268	0.797
RS	PSD	100.260 ± 1.138	1.552	100.08 ± 1.457	0.920
(n = 4)	CTZ	100.700 ± 0.954	0.858	100.37 ± 1.537	0.540
Batch-I	PSD	100.260 ± 1.135	1.138	102.30 ± 1.205	1.457
(n = 4)	CTZ	99.960 ± 1.074	0.954	100.08 ± 1.531	0.985
Batch-II	PSD	98.730 ± 0.762	1.572	99.58 ± 0.792	1.274
(n = 4)	CTZ	97.342 ± 1.077	1.305	99.228 ± 0.692	1.435

SD: standard deviation, %; SE: per cent standard error, CI (confidence interval within which true value may be found at 95% confidence level) = $R \pm ts/\sqrt{n}$; R : result of analysis as mean per cent label claim of authentic samples or recovery or tablet samples; t: theoretical 't' values at 95% confidence level for n – 1 degrees of freedom are t(0.05, 3) = 3.182, t(0.05, 6) = 2.447.

RESULTS AND DISCUSSIONS

The modalities adopted in experimentation were successfully validated as per standard analytical procedures. Prior to analysis of commercial formulations both methods were validated by preliminary analysis of mixed standards containing both drugs in different ratio and authentic laboratory samples. Precise and accurate results were obtained with samples containing 300–1200 μg/mL of PSD. Recovery studies were also carried out. The results of analysis of authentic samples and the average recoveries obtained in each instance were compared with theoretical value of 100 per cent by means of Student's t-test at a 95 per cent confidence level. Recovery studies show that the recoveries obtained for each drug do not differ significantly from 100 per cent and there was no interference from common adjuvants used in the formulation indicating accuracy and reliability of both methods. The results of analysis of commercial formulations are found to be satisfactory as per the label claim with standard deviation values below 1.5 (Table-1).

Both the proposed methods have been found to be accurate, simple, convenient, well in agreement with each other and are suitable for routine analysis in the laboratory. However, the second method, based on absorbance difference and its correlation with interfering absorbance value is comparatively new and innovative, which simplifies the quantification of drugs in combination and shows their adherence to sensitivity, accuracy and precision.

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