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Spectrophotometric method for the determination of pseudoephedrine in bulk and formulations

Krishnamoorthy Balamurugan*, Kannan Gokulakrishnan

PRIST University, Department of Chemistry, East Campus, Thanjavur - 613 403, Tamil Nadu, (INDIA)

E-mail : kbalmurugan@hotmail.com; nandhu_gokul@yahoo.com

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ABSTRACT

A sensitive, extraction, derivatizatation, evaporation and complexation free, direct spectrophphotometric method is developed for the determination of Pseudoephedrine (PE) in bulk drugs and pharmaceutical preparation. The optimum conditions for the analysis of the drug are established. The method permits the determination of PE over a concentration range of 2.5 µg/ml - 12.5 µg/ml. Detection and quantification limits are calculated. The obtained results showed good recoveries of 98.5 with relative standard deviation of 0.5. The repeatability and reproducibility of PE in methanol is determined. Precision and accuracy of the developed method is used for recovery study. The proposed method is applicable for the assay of PE investigation in dosage forms and the results are in good agreement.

KEYWORDS

Pseudoephedrine;
Spectroscopy;
Determination.

INTRODUCTION

Pseudoephedrine (commonly abbreviated as PE) (R*, R*)-2-methylamino-1-phenylpropan-1-ol is a Sympathomimetic amine commonly used as a decongestant. The salts pseudoephedrine hydrochloride and pseudoephedrine sulfate[1-7] are found in many over-the-counter preparations either as single-ingredient preparations. Consumers often refer to it by a product which contains pseudoephedrine, such as Sudafed, the trademark for a common brand of pseudoephedrine hydrochloride in North America. Unlike antihistamines, which modify the systemic histamine-mediated allergic response, pseudoephedrine only relieves nasal congestion commonly associated with colds or allergies. The advantage of oral pseudoephedrine over topical nasal preparations, such as oxymetazoline, is that it does not cause rebound congestion (rhinitis medicamentosa); however, it is more likely to cause adverse effects including hypertension[8-10].

EXPERIMENTAL

Apparatus

A double-beam spectrophotometer Shimadzu UV 1800 model was used.

Chemicals and reagents

Pseudoephedrine pure sample was supplied by a research institution as gift sample and used as such. Pharmaceutical dosage forms were procured from local pharmacies: Methanol used was spectroscopy grade

from Merck India.

Standard solutions

(1) Stock solution

A methanolic primary stock solution of Pseudoephedrine (100 mg) was prepared in methanol and stored in the dark in a refrigerator. All the measurements were performed at room temperature. The standard solutions were prepared by the proper dilution of the primary stock solution with methanol to obtain working standard. For linearity study, serial dilutions were made for Pseudoephedrine in the range of 2.5 to 12.5 µg/ml concentrations were prepared by diluting the stock solution with methanol. The absorbances of these solutions were fitted in the calibration curve to calculate the accuracy and precision of the method.

(2) For formulation

The average weight of the tablets were determined by weigh 20 tablets and powdered. Tablet powder equivalent to 25 mg of PE was weighed and transferred to a 100 ml volumetric flask. About 60 ml of methanol was added and sonicated for 15 minutes complete dissolution of drugs, made up to the volume with methanol and filtered through filter paper. Dilutions were made with methanol to attain a concentration of 10 µg/ml and spectra was recorded. Six replicates of analysis were carried out with sample weighed individually. The average weight of the tablet was found to be 0.19 g.

METHOD VALIDATION

Linearity

The method was validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the Linearity, sensitivity, precision, and accuracy of the analyte. For PE five point calibration curves were generated with the appropriate volumes of the working standard solutions for UV methods. The linearity was evaluated by the least-squares regression method using unweighted data[11-14].

Precision and accuracy

Precision is the degree of repeatability of an analytical method under normal operational conditions. The precision and accuracy were determined with standard quality control samples (in addition to calibration standards) prepared in triplicate at different concentration levels covering the entire linearity range. The precision of the assay was determined by repeatability (intraday) and intermediate precision (inter-day) and reported as RSD % for a statistically significant number of replicate measurements. The intermediate precision was studied by comparing the assays on three different days and the results are documented as the standard deviation and RSD %. Accuracy is the percent of analyte recovered by assay from a known added amount. Data from nine determinations over three concentration levels covering the specified range were obtained.

LOD and LOQ

The limit of detection (LOD) is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from back-ground levels. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve using the following equations LOD = 3s/m; LOQ = 10s/m.

Where s, the noise of estimate, is the standard deviation of the absorbance of the sample and m is the slope of the related calibrations graphs. The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy, precision, and variability. The values of LOD and LOQ were given in TABLE 1.

Stability

The stability of Pseudoephedrine in methanolic solution was studied by the UV method. Sample solutions were prepared in triplicate and stored at 4 and 25°C for 12, 24, 26, 48, 60, and 72h. The stability of these solutions was studied by performing the experiment and looking for the change in the spectrophotometric pattern compared with freshly prepared solutions.

Recovery study

Recovery of the analyte of interest from a given matrix can be used as a measure of the accuracy or the bias of the method. The same range of concentrations as employed in the linearity studies was used. To study the accuracy, precision, and reproducibility of the proposed method and dosage forms, recovery experiments

were carried out using the standard addition method. These studies were performed by the addition of known amounts of pure PE to the pre-analyzed tablet formulation and the mixtures were analyzed using the proposed techniques. After parallel analyses, the recovery results were calculated using the related calibration equations.

RESULTS AND DISCUSSION

The development of a simple, rapid, sensitive, and accurate analytical method for the routine quantitative determination of samples will reduce unnecessary tedious sample preparations and the cost of materials and manpower. PE is a UV-absorbing molecule with specific chromophores in the structure that absorb at a particular wavelength and this fact was successfully employed for their quantitative determinations using the UV spectrophotometric method. The absorption spectrum of PE in methanolic solution is shown in figure 1.

Calibration curves

Calibration curve data was constructed in the range of the expected concentrations of 2.5 – 12.5 µg/ml. Beer's law was obeyed over this concentration range. The regression equation was found to be y = 69.27x – 0.0057. The correlation coefficient (r) of the standard curve was found to be greater than 0.999. The stock solutions and working standards were made in methanol. The λmax of the drug for analysis was determined by taking scans of the drug sample solutions in the entire UV region. The characteristic of the calibration plot is presented in Table 1 and the analytical characteristics and necessary validation parameters for the UV techniques for PE is presented.

Performing replicate analyses of the standard solutions was used to assess the accuracy, precision, and reproducibility of the proposed methods. The selected concentration within the calibration range was prepared in methanol and analyzed with the relevant calibration curves to determine the intra- and interday variability. The intra- and interday precision were determined as the RSD %. The precision, accuracy, and reproducibility of the results given in TABLE 1 and 2 demonstrate a good precision, accuracy, and reproducibility. The proposed methods can be successfully applied for PE assay in tablet dosage forms without any interference. The assay showed the drug content of this product to be in accordance with the labeled claim (TABLE

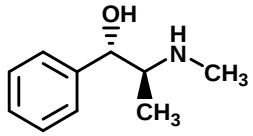

Figure 1 : The structural formula of Pseudoephedrine

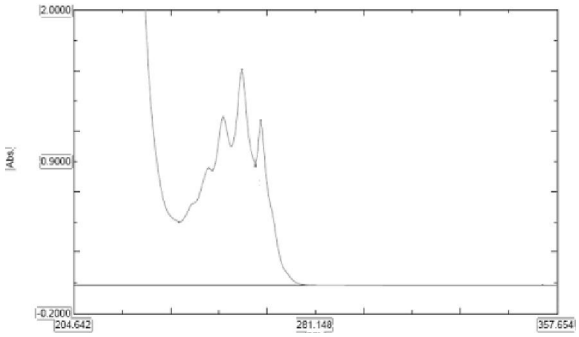

Figure 2 : Absorption spectrum of Pseudoephedrine

TABLE 1 : Regression data of the calibration lines for quantitative determination of PE by UV method

Parameters	Pseudoephedrine
Measured wavelength (λmax)	254
Linearity range, µg/ml	2.5 – 12.5
Slope	69.27
Intercept	-0.0057
Correlation coefficient (r)	0.999
SE of slope	10.14×10^{-2}
SE of intercept	6.5×10^{-4}
LOD, µg/ml	0.0114
LOQ, µg/ml	0.039
Repeatability of absorbance, RSD%	0.17
Repeatability of wavelength, RSD%	0.20
Reproducibility of absorbance, RSD %	0.35
Reproducibility of wavelength, RSD %	0.07

TABLE 2 : Assay results from PE tablets and mean recoveries in spiked tablets

Parameters	Pseudoephedrine
Labelled claim, mg	50
Amount found, mg*	49.82
RSD %	2.87
Added, %	50, 75, 100
Found, %**	98.55, 98.50, 98.45
Recovery, %	98.50
RSD, % of recovery	0.5

***Mean of six determinations, ** three determinations**

2). The recovery of the analyte of interest from a given matrix can be used as a measure of the accuracy of the method (TABLE 2). In order to check the accuracy and precision of the developed method and to prove the absence of interference by excipients, recovery studies were carried out after the addition of known amounts of the pure drug to various pre-analyzed formulations of all drugs. The application of this procedure is explained in the experimental section. The obtained results demonstrate the validity and accuracy of the proposed method for the determination of all drugs in tablets (TABLE 2). These results reveal that the developed method have an adequate precision and accuracy and consequently, can be applied to the determination of PE tablet in pharmaceuticals without any interference from the excipients. The stability of PE in methanolic solution was evaluated to verify that any spontaneous degradation occurs when the samples were prepared. Figure 2 shows that the stability profile at 4 and 25°C for 12, 24, 48, 60, and 72 h. the results were expressed as a percentage of the drugs remaining. The obtained data showed that the sample solutions were stable during 60 h when stored at 4 and 25°C with a degradation of less than 5%. PE was less stable at 25°C with degradation of 3.9% after 72 h.

CONCLUSIONS

A spectrophotometric method for quantifying Pseudoephedrine in formulation samples has been developed and validated. The assay is selective, precise, accurate and linear over the concentration range studied. Pseudoephedrine can be estimated as low as 3.9×10^{-2} µg/ml in formulation could be precisely quantified and LOD was approximately 1.14×10^{-2} µg/ml in formulation. In summary, the proposed method can be used for the drug analysis in routine quality control.

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