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Spectrophotometric Determination of Guaifenesin and Pseudoephedrine Hydrochloride in Tablet Dosage Form

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ABSTRACT

Two simple, accurate, precise, reproducible, requiring no prior separation and economical procedures for simultaneous estimation of guaifenesin and pseudoephedrine hydrochloride in tablet dosage form have been developed. First method is simultaneous equation method; in this method 272 nm and 257 nm were selected to measure the absorbance of guaifenesin and pseudoephedrine hydrochloride respectively. The second method is Q-value analysis based on measurement of absorptivity at 265.50 nm (as an iso-absorptive point) and 272 nm. guaifenesin and pseudoephedrine hydrochloride at their respective maximum wavelength 272 nm and 257 nm and at isoabsorptive point 265.50 nm shows linearity in a concentration range of 30-150 g/mL and 300-1500 g/mL respectively. Recovery studies range from >98.50% for guaifenesin and >98.90% for pseudoephedrine hydrochloride in case of simultaneous equation method and >98.24% for guaifenesin and >98.09% for pseudoephedrine hydrochloride in case of Q-analysis method confirming the accuracy of the proposed method. The proposed methods are recommended for routine analysis since it is rapid, simple, accurate and also sensitive and specific (no heating and no organic solvent extraction is required).

KEYWORDS

Guaifenesin, Pseudoephedrine hydrochloride, Simultaneous equation method, Q analysis.

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INTRODUCTION

Guaifenesin (FIG.1A)[1,2] (RS)-3-(2-methoxyphenoxy) propane-1, 2-diol is an expectorant and widely used in the treatment of coughing [3]. Pseudoephedrine hydrochloride (FIG.1B)[1,2] is (S, S)-2-methylamino-1-phenylpropan-1-ol hydrochloride is a sympathomimietic drug. It is used as a nasal/sinus decongestant and stimulant, or as awakefulness-promoting agent[3].

A **B**

Fig 1: (A) Structure of Guaifenesin, (B) Structure of Pseudoephedrine hydrochloride.

Various spectrophotometric[6-8], HPLC[9, 10], Electrokinetic chromatography[11], Voltammetric assay[12], Capillary gas chromatography[13] and ion pair high performance liquid chromatography[14] methods are also reported in the literature for the estimation of Guaifenesin and Pseudoephedrine individually and in combination with other drugs. According to literature survey no UV method has yet been reported for simultaneous estimation of guaifenesin and pseudoephedrine hydrochloride in tablet dosage forms. Hence, an attempt has been made to develop and validate in accordance with ICH guidelines. [4, 5]

MATERIAL AND METHOD

Pharmaceutically pure sample of guaifenesin was obtained from Global Pharma Mumbai, and pseudoephedrine hydrochloride was obtained from Schon Pharmaceuticals Indore as gift samples along with their analytical reports. Methanol AR grade was obtained from Merck chemical division, Mumbai and Commercial tablet of Guaifenesin (600mg), and Pseudoephedrine hydrochloride (60mg), Mucinex D (Reckitt Benckiser) were procured from the local drug market.

INSTRUMENTATION

A double beam UV-visible spectrophotometer (SHIMADZU, Japan), model UV-1700 PC was used. The software employed was UV probe version 2.33. The spectra was recorded over range 200-400nm against solvent in 1 cm quarts cells.

PREPARATION OF STANDARD STOCK SOLUTIONS

Accurately weighed 100 mg of guaifenesin and 200 mg of pseudoephedrine hydrochloride were transferred into 100 ml volumetric flasks separately and dissolved in 50 ml of methanol and then volume was made up to 100 ml with methanol to get a concentration of 1000 µg/ml for Guaifenesin and 2000 µg/ml for pseudoephedrine hydrochloride. Standard stock solution (1000 µg/ml of guaifenesin and 2000 µg/ml of pseudoephedrine hydrochloride) was further diluted with methanol to obtain 30-150µg/ml for guaifenesin, and 300-1500µg/ml for pseudoephedrine hydrochloride.

DETERMINATION OF MAXIMUM WAVELENGTH AND ISOABSORPTIVE POINT

Working standard solution from the standard stock solution prepared as stated above of 60 g/ml of guaifenesin and 600 g/ml of pseudoephedrine hydrochloride were scanned in the spectrum mode over the range of 200-400 nm against methanol as blank and the overlain spectra of the two were recorded. Guaifenesin showed an absorbance peak at 272 nm whereas pseudoephedrine hydrochloride shows an absorbance peak at 257 nm. The overlain spectra also showed isoabsorptive points at 265.50 nm (FIG 2). Due to difference in absorbance maxima and having no interference with each other so both drug can be simultaneously estimated by simultaneous equation method (Method-1) and absorbance ratio method (Method-II).

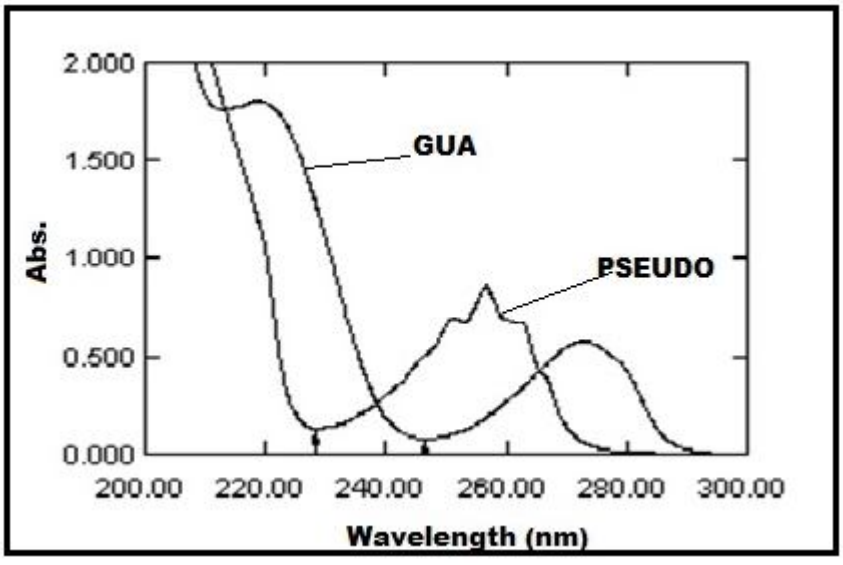

Fig. 2: Overlay spectra of Guaifenesin and Pseudoephedrine hydrochloride

METHOD I (SIMULTANEOUS EQUATION METHOD)

Two wavelengths selected for the method are 272 nm and 257 nm that are absorption maxima of guaifenesin and pseudoephedrine hydrochloride respectively in methanol. The stock solutions of both the drugs were further diluted separately with methanol to get a series of standard solutions of 30-150µg/ml for guaifenesin, and 300-1500µg/ml for pseudoephedrine hydrochloride. The absorbances were measured at the selected wavelengths and absorptivities (A 1%, 1 cm) for both the drugs were determined as mean of five independent determinations. Concentrations in the sample were obtained by using following equations.

$$Cx = (A_2ay_1\text{-}A1ay2)/ (ax_2ay_1\text{-}ax1ay_2)$$

$$Cy = (A_1ax_2\text{-}A_2ax_1)/ (ax_2ay_1\text{-}ax_1ay_2)$$

Where A_1 and A_2 are absorbance of mixture at 272 nm and 257 nm respectively, ax_1 and ax_2 are absorptivities of pseudoephedrine hydrochloride at λ_1 and λ_2 respectively and ay_1 and ay_2 are absorptivities of guaifenesin at at λ_1 and λ_2 respectively. Cx and Cy are concentration of pseudoephedrine hydrochloride and guaifenesin respectively.

METHOD II (ABSORBANCE RATIO METHOD)

From the overlain spectrum of pseudoephedrine hydrochloride and guaifenesin, two wavelengths were selected one at 265.50 nm which is the isoabsorptive point for both the drugs and the other at 272 nm which is λ max of guaifenesin. The absorbances of the sample solutions are prepared in a similar manner as in the previous method, were measured and the absorbance ratio values for both the drugs at selected wavelengths were also calculated. The method employs Q-values and the concentrations of drugs in sample solution were determined by using the following formula,

$$C_{PSE} = \frac{Qm - Qy\,A_1}{Qx - Qyax_1}$$

$$C_{GUA} = \frac{Qm - Qx\,A_2}{Qy - Qx\,ay_1}$$

Where, A_1 and A_2 are the absorbances of mixture at 265.50 nm and 272 nm and ax_1, ax_2 and ay_1, ay_2 are absorptivities E (1%, 1 cm) of pseudoephedrine hydrochloride and guaifenesin at 265.50 nm and 272 nm and $Qm= A_2/A_1$, $Qy = ay_2/ay_1$ and $Qx = ax_2/ax_1$.

VALIDATION OF THE METHOD

Method was validated accordance to ICH guidelines for linearity, precision, accuracy and robustness.

Linearity

The mixed standard stock solution (1000 µg/ml of guaifenesin and 2000 µg/ml of pseudoephedrine hydrochloride) was further diluted to get guaifenesin and pseudoephedrine hydrochloride concentration in the range of 30-150 µg/ml and 300-1500 µg/ml respectively. The resultant absorbances of the drugs were measured. Calibration curve was plotted between absorbance of drug against concentration of the drug. These results shown there was an excellent correlation between absorbance and analyte concentration.

Precision

To evaluate precision at different parameter like repeatability, intermediate precision, five dilutions in three replicates were analyzed in same day, in two different days by two analysts for day to day and analyst to analyst variation.

Robustness of the method

As per ICH norms, small, but deliberate variations by altering the pH and / or concentration of the solvent were made to check the methods capacity to remain unchanged. The change was made in the ratio of solvent. Instead of 100%, 95% methanol was used as solvent.

Recovery studies

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100% and 120%. The recovery studies were carried out by adding known amount of standard solution of guaifenesin and pseudoephedrine hydrochloride to preanalyzed tablet solutions. The resulting solutions were then re-analyzed by proposed methods. Whole analysis procedure was repeated to find out the recovery of the added drug sample. This recovery analysis was repeated at 3 replicate of 3 concentrations levels.

ANALYSIS OF MARKETED FORMULATION

Twenty tablets were taken and their average weight was determined. They are crushed to fine powder; amount equal to 100 mg of Guaifenesin was taken in 100-ml volumetric flask. The amount of Pseudoephedrine hydrochloride present in this tablet powder was 2.0mg; both drugs are in the ratio of 10:1. Then 80 ml of methanol was added and the flask was sonicated for about 10 min to solubilize the drug present in tablet powder, after that drug solution was filtered through Whatman filter paper No. 41. The filtrate was collected and the volume was made up to the mark with methanol. This

solution was used to prepare samples of different concentration of both drugs in the working range. Now all the tablet samples was scanned in multi photometric mode and the concentration of both drugs were obtained from the equation.

RESULTS AND DISCUSSION

The simultaneous equation method and Q-value analysis for estimation of guaifenesin and pseudoephedrine hydrochloride in tablet dosage form was found to be simple, precise, accurate and reproducible. The solvent used was 100% methanol and do not shows any significant interference in the spectrophotometric assay of both drugs.

LINEARITY

The proposed method was found to be linear in the range of 30-150µg/ml and 300-1500µg/ml with correlation coefficient 0.9997 and 0.9998 for guaifenesin (GUA) and pseudoephedrine hydrochloride (PSE) respectively. Result of linearity study shown in Table 1.

TABLE 1: RESULTS OF LINEARITY

Parameters	Method - I		Method-II	
	GUA	PSE	GUA	PSE
Working λ	272 nm	257 nm	272 nm	265.50nm
Beer's law limit (g/ml)	30-150	300-1500	30-150	300-1500
Correlation Coefficient (r^2)*	0.9997	0.9998	0.9997	0.9998
Slope (m)*	0.044	0.006	0.035	0.006
Intercept (c)*	0.001	0.002	-0.001	0.002

* Average of five determination

RECOVERY STUDIES

TABLE 2: RESULTS OF RECOVERY STUDIES

Recovery Level%	% Recovery (Mean ±SD)*			
	Method - I		Method-II	
	GUA	PSE	GUA	PSE
80	96.70±0.20	99.10±0.17	98.50±0.06	97.59±0.35
100	98.50±0.06	98.90±0.23	98.24±0.09	98.09±0.27
120	99.70±0.05	98.40±0.21	95.98±0.06	98.48±0.50

*Average of nine determinations

As shown from the data in Table 2, good recoveries of guaifenesin and pseudoephedrine hydrochloride in the range from 95 to 101% were obtained at various added concentrations.

PRECISION

The results of the repeatability and intermediate precision experiments are shown in (Table 3, 4). The developed method was found to be precise as the RSD values for repeatability and intermediate precision studies were < 2 %, respectively as recommended by ICH guidelines.

ROBUSTNESS OF THE METHOD

Standard stock solution of 1000 µg/ml and 2000 µg/ml of guaifenesin and pseudoephedrine hydrochloride were prepared using 95% methanol as a solvent. From standard stock solution, sub stock solution of 100 µg/ml and 200 µg/ml of guaifenesin and pseudoephedrine hydrochloride were prepared separately. From these standard stock solutions of drugs, appropriate dilutions were prepared to get mixed standard solutions of both drugs. Result of robustness shown in Table 3, 4.

TABLE 3: RESULTS OF PRECISION AND ROBUSTNESS

Parameter		Method - I		Method-II	
		GUA	PSE	GUA	PSE
Precision (Mean±SD)*	Repeatability	97.88±0.05	98.22±0.64	98.64±0.09	99.22±0.49
	Day to Day	98.97±0.06	98.97±0.54	99.42±0.08	98.77±0.40
	Analyst to Analyst	96.82±0.12	96.82±0.44	96.22±0.09	97.77±0.38
	Robustness	99.28±0.04	99.10±0.51	98.47±0.20	99.06±0.61

*Average of nine determinations

TABLE 4: RESULTS OF PRECISION AND ROBUSTNESS (%RSD)

Parameter		Method - I		Method-II	
		GUA	PSE	GUA	PSE
Precision (%R.S.D.)*	Repeatability	0.662	0.643	0.096	0.493
	Day to Day	0.066	0.540	0.080	0.403
	Analyst to Analyst	0.122	0.441	0.092	0.384
	Robustness*	0.049	0.517	0.206	0.617

*Average of nine determinations

ANALYSIS OF A FORMULATION

Experimental results show that there is no interference from any of the excipients which are normally present with that of standard guaifenesin and pseudoephedrine hydrochloride. The drug content was found to be close to 100 for guaifenesin and for pseudoephedrine hydrochloride (Table 5).

TABLE 5: RESULTS OF STATISTICAL PARAMETERS FOR TABLET ANALYSIS

S. NO.	Drug	Label Claim	Amount Found	MEAN*	S.D.*	%COV*	S.E*
Method 1	GUA	600	598.85	99.40	0.187	1.33	0.079
	PSE	60	58.64	98.09	0.780	0.641	0.124
Method 2	GUA	600	598.92	99.39	0.070	0.748	0.013
	PSE	60	59.96	98.91	0.392	0.388	0.011

*Mean of five determinations

CONCLUSIONS

The simultaneous UV method was developed and validated for simultaneous estimation of Guaifenesin and Pseudoephedrine hydrochloride in tablet dosage form. Proposed method is fast, accurate, precise and sensitive hence it can be employed for routine quality control of tablets containing both drugs in industries.

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