Spectrophotometric estimation of guaifenesin and salbutamol in pure and tablet dosage form by using different methods

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ABSTRACT

Two simple, precise, accurate and economical UV spectrophotometric methods have been developed and validated for routine estimation of Guaifenesin and Salbutamol in tablet dosage form. Spectroscopic studies were carried out using double beam U.V.Spectrophotometer model JASCO. The marketed combination of Guaifenesin and Salbutamol that is salbusum forte from Local market. Method A employs formation and solving of simultaneous equation using 274 nm and 279 nm as two analytical wavelengths for both drugs in Distilled water, Whereas Method B involved formation of Q-absorbance equation at isobestic point (253 nm). Guaifenesin and Salbutamol shows Linearity in a concentration range of 10-50μg /ml. Recovery studies for guaifenesin 97.99 % and 99.22 % for salbutamol in case of simultaneous equation method confirming the accuracy of the proposed method.

Keywords: Guaifenesin, Salbutamol, Simultaneous equation method, Q-Absorbance ratio method
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INTRODUCTION

Guaifenesin (FIG.1A) (RS)-3-(2-methoxyphenoxy) propane-1, 2-diol is an expectorant and widely used in the treatment of coughing . It is the glyceryl ether of guaiacol (a constituent of guaiac resin from the wood of Guajacum officinale Linne), it act as expectorant by increasing the volume and reducing the viscosity of secreations in the trachea and bronchi. It is the component of numerous cough cold preparations available worldwide. Salbutamol, RS-[4-[2-(tert-butylamino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol] is a shortacting β2-adrenergic receptor agonist used for the relief of Broncho-spasm in conditions such as asthma and chronic obstructive pulmonary disease.
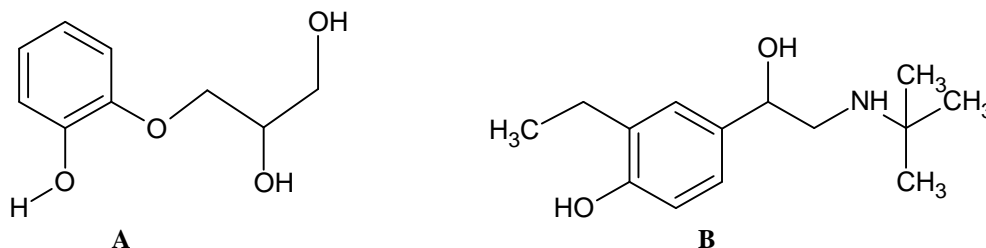

Fig 1: (A) Structure of Guaifenesin, (B) Structure of Salbutamol.

Various spectrophotometric Reverse Phase Liquid Chromatography and Immunoaffinity-chromatography, High performance liquid chromatographic determination is also reported. 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.

92

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MATERIALS AND METHODS

Instrument -
JASCO Double beam UV-VIS Spectrophotometer with spectral band width of 1.8 nm,wavelength accuracy of ±2 nm and matched quartz cells of 10 mm optical path length was used for all spectral and absorbance measurements.

Materials-
A Jasco V-630 UV- Visible double beam spectrophotometer with 1 cm matched Quartz cells were used for spectral measurement. Schimadzu AX 200 Analytical balance was used for weighing purposes. The Reference Standard of Guaifenesin and Salbutamol was taken And tablet was procured from market, Salbusum Forte were utilized for the study. All chemicals and reagent used were of analytical grade.

Method-
Preparation of stock solution-
1. Pure drug-
Accurately weighed 10mg pure drug of GUA and SAL were dissolved in the distilled water in a two different 10ml volumetric flask and sonicated for 10 min.Then from this solution pipette out 1ml from each in separate 10 ml volumetric flask and named as stock solution B. The resultant stock solution contains 100 μg/ml GUA and 100 μg/ml SAL. Appropriate aliquots of the stock solution were withdrawn and serial dilutions were performed.The dilution were prepared such as 10ug, 20ug, 30ug, 40ug, 50ug per 1ml as per its linerity.

2. Marketed formulation-
Twenty tablets were accurately weighed and reduced to fine powder, powder equivalent to 10mg of guaifenesin was weighed and dissolved in 10mL of distilled water in a 100mL volumetric flask, final volume was made with distilled water and sonicated for about 10min. The above solution was filtered by using Whattmann filter paper No.:41. From this solution sufficint aliquotes was pipette out into 10ml volumetric flask and from these serial dilution was prepared.The absosbance values of these solution were measured at 274 nm and 279 nm respectively .

1. Assessment of absorption maxima
The two solutions were scanned separately in the range of 200-400 nm to determine respective wavelength of maximum absorption. GUA and SAL showed absorbance maxima at 274 nm (λ_1) and 279 nm (λ_2) respectively.

Method A:
Simultaneous Estimation Method
GUA and SAL showed absorbance maxima at 274 nm ($\lambda 1$) and 279 nm ($\lambda 2$) respectively. The absorbances were measured at the selected wavelength and absorptivities (A 1%, 1cm) for both the drugs at both wavelengths were determined.

Preliminary calculations and assumptions
1. The absorptivities of GUA at λ_1 and λ_2, ax_1 and ax_2 respectively.
2. The absorptivities of SAL at λ_1 and λ_2, ay_1 and ay_2 respectively.
3. The absorbances of diluted sample at λ_1 and λ_2, A_1 and A_2 respectively.
4. Let Cx and Cy be the concentrations of GUA and SAL respectively in diluted sample.

The two equations were constructed based upon the fact that at λ_1 and λ_2 the absorbance of the mixture is the sum of individual absorbances of GUA and SAL.

At λ_1, $A_1 = ax_1 bcx + ay_1 bcy$ …… (1)
At λ_2, $A_2 = ax_2 bcx + ay_2 bcy$ …… (2)

Where, A_1 and A_2 are absorbances of mixture at 274 nm and 279 nm respectively.

Method B:
Absorption Ratio Method (Q Method)
The solutions of GUA and SAL (10 mcg/ml) were scanned in the range of 100 to 400 nm against distilled water as blank. For Q method, 253 nm (isobestic point) and 279 nm (λmax of GUA) were selected as wavelengths of measurements. Concentrations of GUA and SAL were determined using following equations.

$Cx = (Qm-Qy). A_1 / (Qx-Qy). ax_1$

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$Cy = (Qm-Qx). A_1 / (Qy-Qx). ay_1$

Where
$Qm = A_2/ A_1$
$Qx = ax_2/ ax_1$
$Qy = ay_2/ ay_1$

Where, A_1 and A_2 are absorbance's of mixture at 274nm and 279 nm respectively ax_1 and ax_2 are absorptivities of GUA at λ_1 and λ_2 respectively and ay_1 and ay_2 are absorptivities of SAL at λ_1 and λ_2 respectively. Cx and Cy are concentrations of GUA and SAL respectively.

Validation
The method was validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision and accuracy for the analyte.

Accuracy
The accuracy of the methods was determined by performing recovery studies on tablet formulation and for prepared solutions containing known amount of drug by standard addition method in which preanalyzed samples were taken and standard drug was added at three different levels 80%, 100% and 120% as per ICH guidelines. The recovery study performed three times at each level.Percent recovery for Guaifenesin and Salbutamol by this method was found in the range of 97.99- 99.22%

Linearity
The linearity of measurement was evaluated by analyzing different concentration of the standard solution of Guaifenesin and Salbutamol (figures 1 and 2). For simultaneous equation method the Beer - Lambert's concentration range was found to be 10-50µg/ml for Guaifenesin and 10-50 µg/ml for Salbutamol.

RESULTS AND DISCUSSION

Under experimental conditions described, calibration curve, precision and recovery studies were performed. The drugs obey beer's law in the concentration range 10-50 µg/ml for GUA and 10-50 µg/ml for SAL for all the methods with good correlation coefficient 0.996 and 0.993 respectively.The results of commercial formulation analysis are presented in Table 1. Results of recovery studies are shown in Table 2. The accuracy and reproducibility is evident from the data as results are close to 100 % and low standard deviation. The proposed methods are simple, economical, rapid, precise and accurate. Hence these can be used for routine analysis of GUA and SAL in tablet formulation.

Table 1: Analysis of Tablet formulation

| Drug	Label claim (Mg/ tab.)	Amount found (mg)		%Drug found ±SD		Standard Error	
		Method A	Method B	Method A	Method B	Method A	Method B
GUA	100	99.63	99.57	99.63±0.30	99.57±0.35	0.14	0.11
SAL	2	1.98	1.95	99±0.20	97.5±0.18	0.085	0.079

Values expressed mean± SD (n=6)

Table 2: Recovery study of GUA AND SAL

Drug	Level of addition (%)	Amount added (µg/ml)	Amount recovered (µg/ml)		%Recovery ± SD	
			Method A	Method B	Method A	Method B
GUA	80	4	3.87	3.86	96.75± 0.056	96.5 ± 0.044
	100	5	4.97	4.95	99.4 ± 0.049	99.00 ± 0.042
	120	6	5.87	5.90	97.83 ± 0.069	98.33 ± 0.055
SAL	80	4	3.97	3.98	99.25 ± 0.083	99.5 ± 0.077
	100	5	4.98	4.92	99.6 ± 0.044	98.4 ± 0.043
	120	6	5.93	5.94	98.83 ± 0.045	99.00 ± 0.035

Values expressed mean± SD (n=3)

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Table 3: Optical characteristics data and validation parameters

Parameters	For Guaifenesin Values	For Salbutamol values
Absorption maxima (λ max)	274 nm	279 nm
Beer's law limit (µg/ml)	10-50	10-50
Regression equation	Y = 0.012x + 0.010	Y= 0.008x - 0.010
Correlation coefficient (r^2)	0.996	0.993
Accuracy (%Recovery ± SD)	97.99± 0.058	99.22 ±0.057
Precision		
Intraday*(Analyst 1)	99.31±0.35	99.75±0.2
Interday*(Analyst 2)	100.86±0.86	98.66±0.81
LOD (µg/ml)	0.2831	0.1429
LOQ (µg/ml)	0.7735	0.4327

$y = 0.012x + 0.010$
$R^2 = 0.999$
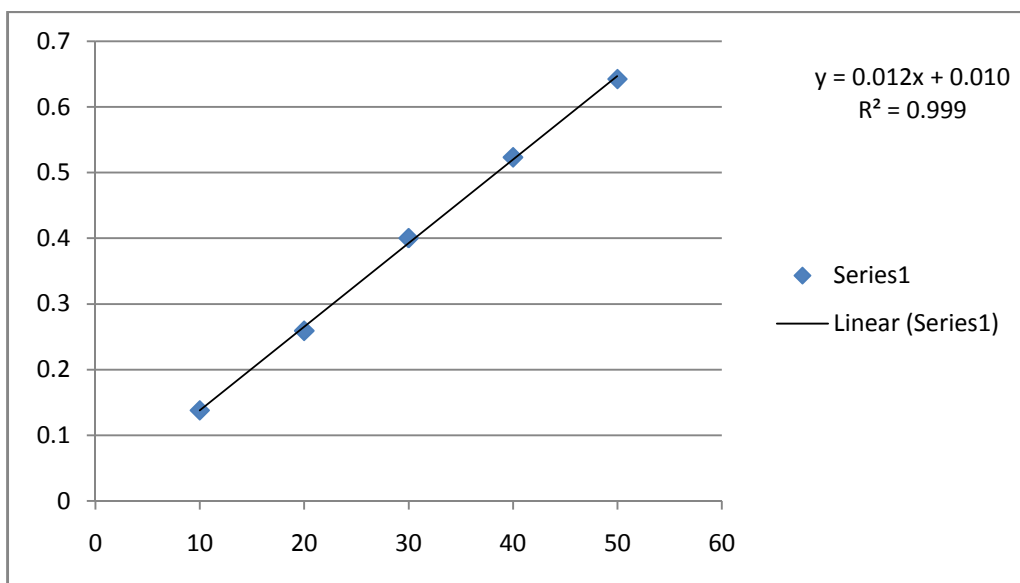
Fig. 2: Linearity curve for Guaifenesin

$y = 0.008x - 0.010$
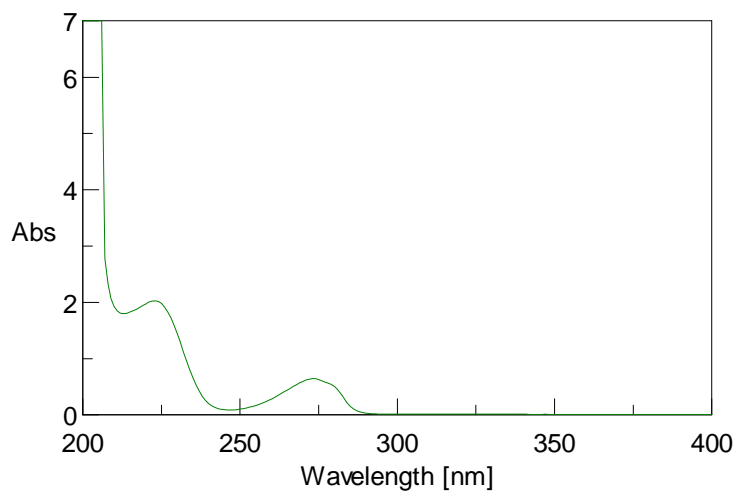$R^2 = 0.993$
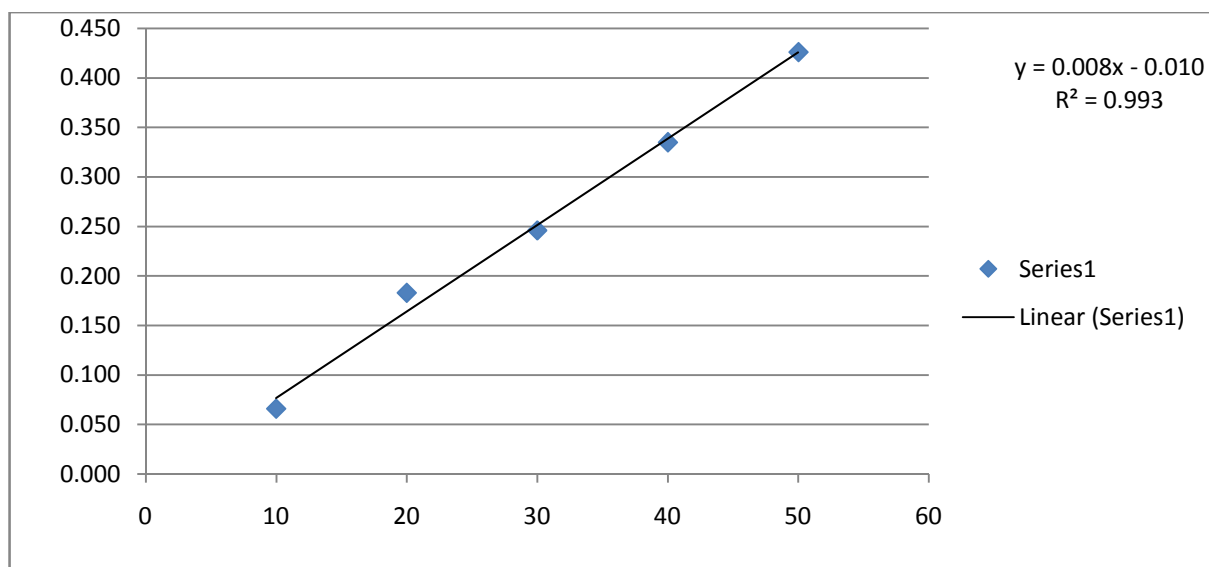
Fig. 3: Linearity curve for Salbutamol

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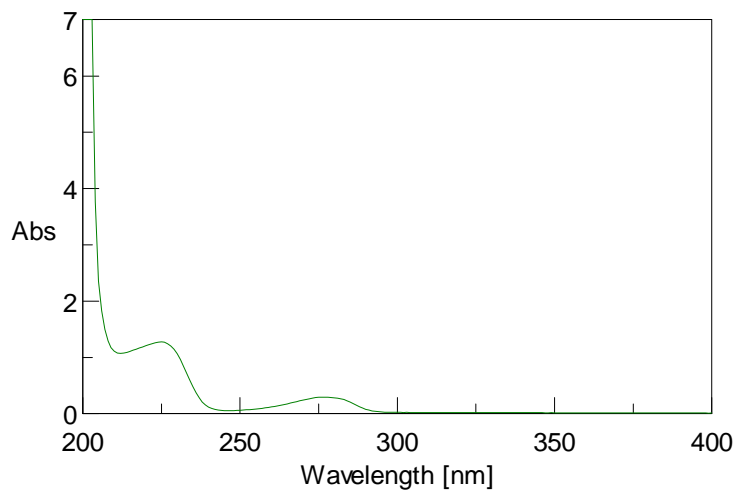**Fig.4 Graph of Guaifenesin API**

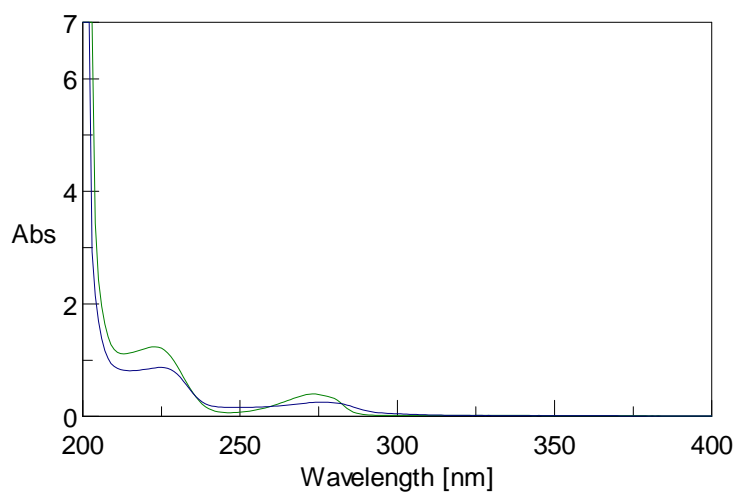**Fig.5 Graph of Salbutamol API**

Fig.6 Graph Of Overlay Spectra Of Guaifenesin and Salbutamol API

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CONCLUSION

The method for the determination of Guaifenesin and Salbutamol have been developed and validated. The Method is applicable over a range of 10-50µg/ml for GUA and 10-50 µg/ml for SAL.The developed method was found to be simple, sensitive, accurate, precise, cost effective, reproducible, and can be used for routine quality control analysis in tablet dosage form.

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