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Research Article

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Simultaneous spectrophotometric estimation of ambroxal hydrochloride and guaiphenesin by first order derivative method in combined dosage form

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ABSTRACT

The objective of the study was to develop a simple, accurate, precise and rapid a UV spectrophotometric i.e. first order derivative method for the determination of ambroxal hydrochloride and guaiphenesin in combined dosage form i.e. tablets by using distilled water as a solvent. The method was further validated by ICH guidelines. The proposed first order derivative method involves the measurement of absorbance of one drug at zero crossing point of other; hence wavelengths 216 nm and 264 nm were selected for the estimation of ambroxal hydrochloride and guaiphenesin respectively. The linearity of the proposed method was found in the concentration range of 1 to 10 µg /ml (r^2= 0.9998) for ambroxal hydrochloride and 10 to 100 µg /ml (r^2= 0.9999) for guaiphenesin respectively. The percentage mean recovery was found to be 99.885 % for ambroxal hydrochloride and 99.935 % for guaiphenesin respectively. The method was also statistically validated for its linearity, accuracy and precision. Both intra and inter day variations showed less percentage (%) RSD values indicating high grade of precision of this method.

Keywords: UV spectrophotometric estimation, First order derivative method, Ambroxal hydrochloride, Guaiphenesin

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INTRODUCTION

Ambroxal Hydrochloride is trans-4-[(2Amino-3,5-dibromobenzyl)amino] cyclohexanol. It shows molecular formula as $C_{13}H_{18}Br_2N_2O.HCl$ with molecular weight 414.57. It is official in BP [1] and IP [2]. Ambroxal is a metabolite of bromhexine. It is an expectoration improver and mucolytic agent used in the treatment of acute and chronic disorders characterized by the production of excess or thick mucus.

Guaiphenesin is, 3-(2-Methoxyphenoxy)-1,2-propanediol. It shows molecular formula as $C_{10}H_{10}O_4$ with molecular weight as 198.2. It is official in BP [1] and IP [2] and USP [3] is used to increase the volume and reduce the viscosity of tenacious sputum and is used as expectorant for productive cough.

In literature survey reveals UV spectrophotometric method [4] for simultaneous determination of ambroxal hydrochloride and guaiphenesin in combined dosage form.

EXPERIMENTAL SECTION

Instrument and reagents

Spectral scan was made on a Shimadzu UV-spectrophotometer, model 1800 (Shimadzu, Japan) with spectral band width of 0.5 nm with automatic wavelength corrections by using a pair of 10 mm quartz cells. All spectral measurements were done by using UV-Probe 2.42 software.

Reference standard of ambroxal and guaiphenesin were obtained from reputed firm with certificate of analysis.

Preparation of standard drug solutions

A 100 mg standard ambroxal hydrochloride was weighed accurately and transferred to a 100 ml volumetric flask and sonicated with 30 ml distilled water for 15 minutes. The volume was made up to the mark with distilled water to give a stock solution of ambroxal hydrochloride of concentration 1000 µg /ml. From this solution, 10 ml of solution was pipetted out and transferred into 100 ml volumetric flask. The volume was made up to mark with distilled water to give a working standard solution of concentration 100 µg/ml.

Similarly 100 mg standard guaiphenesin was weighed accurately and transferred to a 100 ml volumetric flask and sonicated with 30 ml of distilled water for 15 minutes. The volume was made up to the mark with distilled water to give a stock solution of distilled water of concentration 1000 µg /ml. From this solution, 10 ml of solution was pipetted out and transferred into 100 ml volumetric flask. The volume was made up to mark with distilled water to give a working standard solution of concentration 100 µg/ml.

Estimation from tablets

Twenty tablets were weighed accurately and average weight of each tablet was determined. Powder equivalent to 30 mg of ambroxal hydrochloride and 100 mg of guaiphenesin was weighed and transferred in 100 ml of volumetric flask. A 30 ml of distilled water was added and sonicated for 15 minutes and filtered. The filtrate and washing were diluted up to the mark with distilled water to give concentration as 300 µg /ml of ambroxal hydrochloride and 1000 µg/ml of guaiphenesin respectively. For working sample solution 1 ml of such solution was diluted to 100 ml and such solution was used for analysis.

Method: First order derivative method

(a) For ambroxal hydrochloride

For the selection of analytical wavelength, 100 µg/ml solution of ambroxal hydrochloride was scanned in the spectrum mode from 350 nm to 190 nm by using distilled water as blank. The first order derivative spectrum was obtained by using derivative mode by UV probe 2.42 software. From the spectrum, the amplitude of the derivative spectrum was measured at 216 nm.

(b) For guaiphenesin

For the selection of analytical wavelength, 100 µg/ml solution of guaiphenesin was scanned in the spectrum mode from 350 nm to 190 nm by using distilled water as blank. The first order derivative spectrum was obtained by using derivative mode by UV probe 2.42 software. From the spectrum, the amplitude of the derivative spectrum was measured at 264 nm.

Preparation of calibration curves

Series of solutions containing 1 – 10 µg/ ml of ambroxal hydrochloride and 10 -100 µg/ ml of guaiphenesin were used to determine linearity of the proposed method respectively. Solutions were scanned in the spectrum mode and absorbance spectra were converted to first order derivative spectra. The overlain spectrum of ambroxal hydrochloride and guaiphenesin were given in Fig. 1(a), 1(b) respectively.

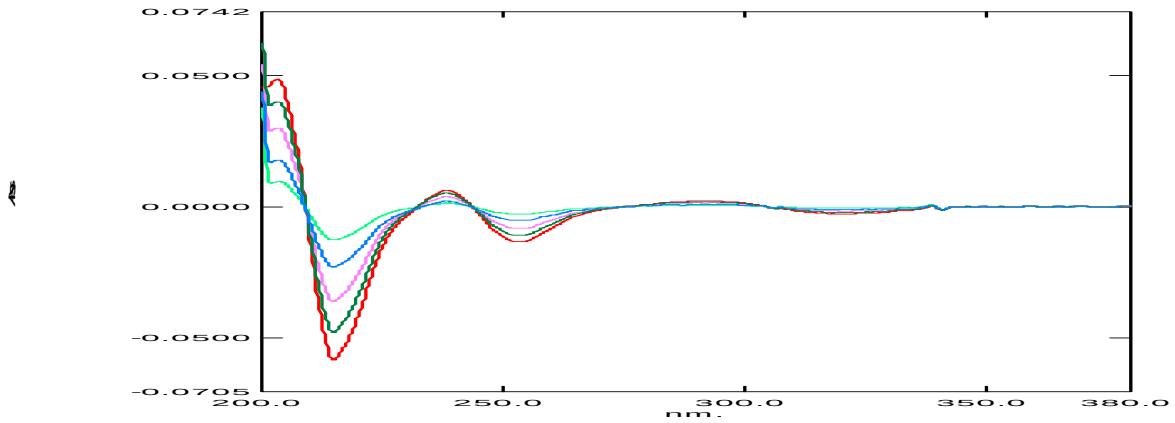

Fig. 1(a): Overlay spectra of first order derivative of ambroxal hydrochloride in the Concentration range of 2– 10 µg/ ml

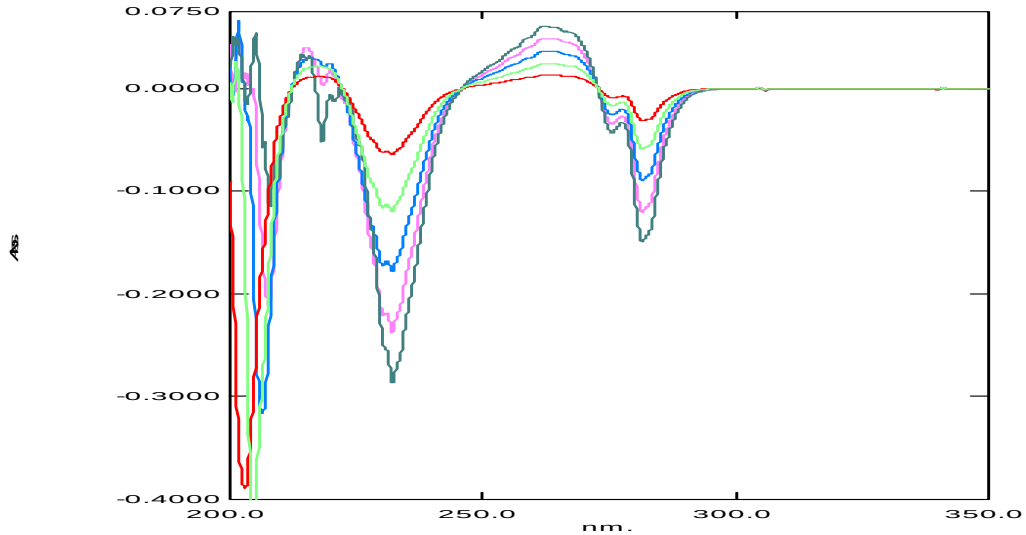

Fig. 1(b): Overlay spectra of first order derivative of guaiphenesin in the concentration range of 20 – 100 µg/ ml

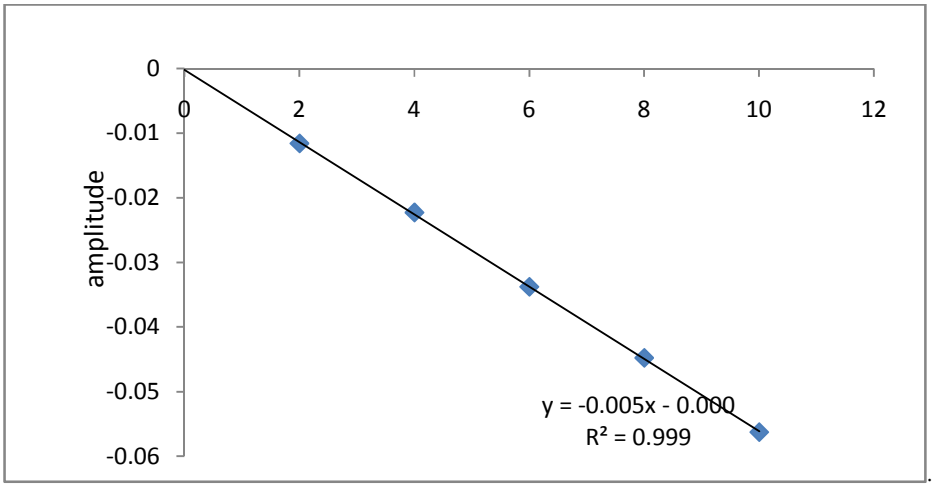

Fig.2 (a): Calibration curve of ambroxal hydrochloride in the concentration range of 2-10 µg/ml

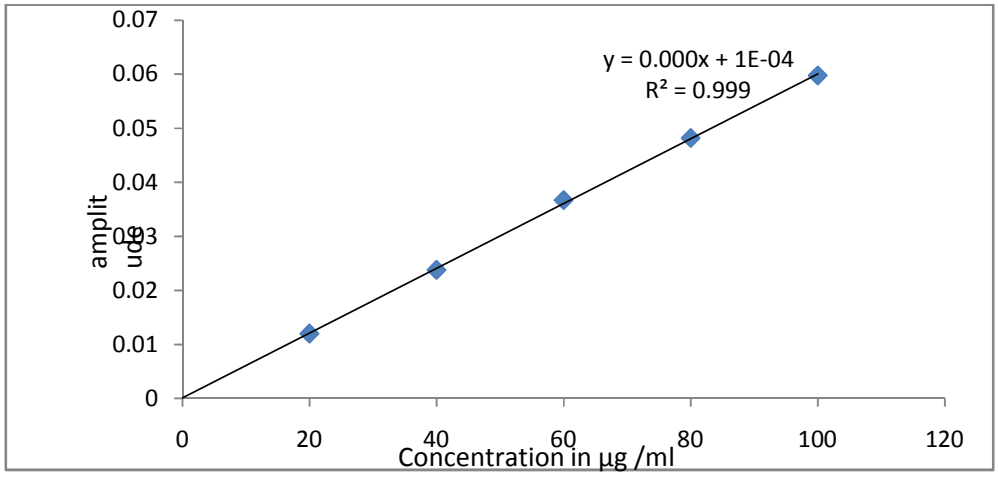

Fig.2 (b): **Calibration curve of guaiphenesin in the concentration range of 10-100 µg/ml**

After observing the overlain first order derivative spectra of ambroxal hydrochloride and guaiphenesin, the zero crossing points of both drugs were selected for analysis of other drug. The first wave length selected was 216 nm, the zero crossing point of guaiphenesin where ambroxal hydrochloride showed considerable absorbance. The second wavelength was 264 nm, the zero crossing point of ambroxal hydrochloride, where guaiphenesin showed considerable absorbance. The calibration curves were plotted of dA/ dλ against concentrations [Fig. 2 (a), 2(b)].

Results of the analysis are given in table 1.

Table 1: Values of results of optical and regression of drugs

Parameter	Ambroxal hydrochloride	Guaiphenesin
Detection Wavelength (nm)	216	264
Beer Law Limits (µg/ml)	10-Feb	10-100
Correlation coefficient(r^2)	0.9999	0.9996
Regression equation (y=b+ac)		
Slope (a)	-0.0056	-0.0002
Intercept (b)	0.0006	-0.0001

Estimation from capsules

Powdered from twenty capsules were collected and weighed accurately and average weight of powder from each capsule was determined. Powder equivalent to 30 mg of ambroxal hydrochloride and 100 mg of guaiphenesin was weighed and transferred in 100 ml of volumetric flask. A 30 ml of distilled water was added and sonicated for 15 minutes and filtered. The filtrate and washing were diluted up to the mark with distilled water to give concentration as 30 µg /ml of ambroxal hydrochloride and 100 µg /ml of guaiphenesin respectively. A 10 ml of such solutions was diluted to 100 ml. It was scanned in the range of 190-350 nm against distilled water as blank. The absorbance spectra were converted to first order derivative spectra. Calculations were done as per the equations. The concentrations of ambroxal hydrochloride and guaiphenesin present in capsules were calculated by substituting the values of absorbance in linearity equations.

(a) For ambroxal hydrochloride Y = -0.0056x - 0.0002
(b) For guaiphenesin Y = -0.0006x - 0.00001

Method Validation

These methods were validated according to ICH guidelines.

Accuracy

To ascertain the accuracy of proposed methods, recovery studies were carried out by standard addition method at

three different levels (80%, 100% and 120%). Percentage recovery for ambroxal hydrochloride and guaiphenesin was found in the range of 99.630 % to 99.95% and 99.736% to 100.11 % respectively. (Table2).

Table 2: Statistical evaluation of the data subjected to accuracy

Level of % recovery	Amount present in µg/ml		Amount added in µg/ml		Amount found in µg/ml		% Recovery		Mean % recovery	
	AMB	GUI	AMB	GUI	AMB	GUI	AMB	GUI	AMB	GUI
80%	3.0	10	2.4	8	5.3956	17.863	99.92	99.24	99.95	99.736
	3.0	10	2.4	8	50392	18.014	99.87	100.08		
	3.0	10	2.4	8	5.4032	17.980	100.06	99.89		
100%	3.0	10	3.0	10	6.0048	19.964	100.08	99.88	99.91	99.97
	3.0	10	3.0	10	5.9802	19.974	99.87	100.14		
	3.0	10	3.0	10	5.9860	19.978	99.78	99.89		
120%	3.0	10	3.6	12	6.5267	22.026	98.80	100.12	99.63	100.11
	3.0	10	3.6	12	6.6033	22.033	100.15	100.28		
	3.0	10	3.6	12	6.5927	21.986	99.94	99.94		

AMB = Ambroxal hydrochloride, GUI = Guaiphenesin

Linearity

The linearity of measurement was evaluated by analyzing different concentration of the standard solutions of ambroxal hydrochloride and guaiphenesin. For both the drugs concentration range was found to be 1-10 µg/ml for ambroxal hydrochloride and 10-100 µg/ml for guaiphenesin.

Precision

The method precision was established by carrying out the analysis of powder blend from capsules containing 30 mg of ambroxal hydrochloride and 100 mg of guaiphenesin. The assay was carried out for the drugs by using proposed analytical method in six replicates. The values of relative standard deviation were 0.1605 % for ambroxal hydrochloride and 0.1033 % for guaiphenesin respectively indicating the sample repeatability of the method. The results obtained are tabulated in table 3**.**

Table 3: Statistical evaluation of the data subjected to method of precision

Sr. No.	Sample No.	% Assay	
		Ambroxal hydrochloride	Guaiphenesin
1	1	100.08	99.88
2	2	99.87	100.14
3	3	99.78	99.89
4	4	99.65	99.87
5	5	100.04	99.94
6	6	99.89	99.89
Mean % assay		99.885	99.935
%R.S.D.		0.1605	0.1033

Intra-day precision was estimated by assaying tablets powder blend containing 30 mg of ambroxal hydrochloride and 100 mg of guaiphenesin. The assay was carried out for the drugs by using proposed analytical method in six replicates. The results were average for statistical evaluation.

Inter-day precision was estimated by assaying tablets powder blend containing 30 mg of ambroxal hydrochloride and 100 mg of guaiphenesin for three consecutive days (i.e. 1st, 3rd and 5th days). The statistical validation data for intra and inter day precision is summarized in table 4.

Table 4: Summary of validation parameter for intra-day and inter-day

Sr. No.	Parameters	Ambroxal hydrochloride	guaiphenesin
1	Intra-day precision (N=3)amount found ± % R.S.D.	99.73% 0.1605	99.55% 0.1033
2	Inter-day precision (N=3)amount found ± % R.S.D.	98.784 0.1359	98.782% 0.1768

Both intra- day and inter-day precision variation found to be less in % RSD values. It indicates high degree of precision of the method.

RESULTS AND DISCUSSION

The developed first order derivative spectrophotometric method for simultaneous determination of ambroxal hydrochloride and guaiphenesin in tablet formulation was found to be simple and convenient for the routine analysis of two drugs. The method is used to eliminate the spectral interference from one of the two drugs while estimating the other drug by selecting the zero crossing point on the derivative spectra of each drug as the selected wavelength. The proposed method is accurate, precise and reproducible. It is confirmed from validation data as given in tables 1 to 4. The % RSD was found to be less than 1, which indicates validity of method. Linearity was observed by linear regression equation method for ambroxal hydrochloride and guaiphenesin in different concentration range. The correlation coefficient of these drugs was found to be close to 1.00, indicating good linearity figure 2 (a) and 2 (b).

The assay results obtained by proposed method is shown in table 2 are in good agreement. Hence proposed method can be used for routine analysis of these two drugs in combined dosage form. Method is simple, accurate, precise, reliable, rapid, sensitive, reproducible and economical. It is validate as per ICH guidelines.

CONCLUSION

The proposed method is simple, precise, accurate and rapid for the determination of ambroxal hydrochloride and guaiphenesin in combined dosage form. This method can be adopted as an alternative to the existing methods. It can be easily and conveniently adopted for routine quality control analysis.

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