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Research Article

SPECTROPHOTOMETRIC METHOD FOR DEVELOPMENT OF GUAIPHENESIN IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

The estimation of Guaiphenesin was based on the reaction of alcoholic solution of 1, 10-phenanthroline (Ferroin indicator) in the presence of ferric chloride. The orange red colour complex formed with ferric chloride and 1, 10-phenanthroline, due to oxidation of Guaiphenesin by ferric chloride and thereby itself undergoing reduction from ferric ion to ferrous ion. Ferrous ion forms a complex with 1, 10-phenanthroline which showed λmax at 510nm.The method obeys Beer-Lambert's law in the concentration ranges of 10-60µg/ml of Guaiphenesin. The methods were validated for linearity, sensitivity, precision, accuracy, robustness and ruggedness.

Keywords: Guaiphenesin, 1, 10-phenanthroline, Ferric chloride, Beer-Lambert's law.

INTRODUCTION

Guaiphenesin is designated chemically as 3-(2-methoxyphenoxy)-1, 2-propanediol[1] with molecular formula $C_{10}H_{14}O_4$ .It is used with antihistamines, decongestants and antitussives in combination product. Guaiphenesin is an only expectorant recognized by the FDA. It increases the volume and reduces the viscosity of secretions in the trachea and bronchi. It also stimulates the flow of respiratory tract secretions, allowing ciliary movement to carry the loosened secretions upward toward the pharynx[2].

Literature survey reveals that Guaiphenesin was assayed by capillary gas Chromatography[3], HPLC[4, 5], LC-MS[6, 7], HPTLC [8], UV spectroscopy [9]. Determinations of Guaiphenesin by colorimetric method in pharmaceutical dosage form have not been reported in literature.

The main objective of this study is to develop a new, fast, reliable and simple method for the

Quantization of Guaiphenesin in marketed formulation with its latter validation study. The method validation was carried out using the parameters proposed by the ICH[10] guidelines.

EXPERIMENTAL

Chemicals and Reagents

Guaiphenesin pure drug was supplied as a gift sample of INDOCO Remedies. Guaiphenesin tablet was purchased from local market. All chemicals and reagent used were of analytical grade and were purchased from Merck Chemicals, India.

Instrumentation

The instrument used was Jasco V-630 spectrophotometer, with 1cm matched quartz cell. Weighing was done on electronic balance (Essae Lmt) and sonicator (PCI Analytes) used for dissolution.

Preparation of standard stock solution of Guaiphenesin (1mg/mL)

Stock solution of Guaiphenesin was prepared by accurately weighing 100mg of pure drug into a 100 ml volumetric flask and dissolved it in 25 ml of methanol and the volume was made up to the mark with methanol to get a concentration of 1 mg/ml. For working standard solution10ml was pipetted out of standard stock solution into a100ml volumetric flask and the volume

was made up to the mark with methanol to get 100 µg/ml.

METHOD

Pure Drug

From standard working solution 1ml (100 µg/ml) were transferred into a series of 10ml volumetric flasks. To each flask 1ml 0.5% of ferric chloride was added, followed by 0.8% of 1ml of 1,10-phenanthroline and kept aside for 10mins for the completion of reaction and volume was made up to 10ml with methanol. The absorbance of orange red colored chromogen was measured at 510nm against corresponding reagent blank.

Analysis Of Marketed Formulation

20 tablets of Barkeit (marketed product) containing 200mg Guaiphenesin was obtained for all analytical study. Powder equivalent to 100mg of Guaiphenesin was weighed accurately and transferred into 100 ml volumetric flask. The volume was made up to 100ml using methanol. The flask was shaken and volume was made up to the mark with methanol to give a solution of 1000 µg/ml (Stock Solution A).From the above Stock solution A, 1ml was pipetted out and added to a 100
ml volumetric flask. (Stock solution B).From the stock solution B, 1ml was pipetted into 10ml volumetric flask. To this 0.5 ml of 0.5 % Ferric chloride was added followed by 1 ml of 0.8 % of 1,10-Phenanthroline. The reaction mixture was kept aside for 15 min for the completion of
reaction and after 15min, the volume was made up to 10 ml with methanol. The blank was also prepared simultaneously in the same way omitting the drug. The absorbances of the resulting solutions were measured at 510nm against reagent blank. (Table no: 1)

VALIDATION PARAMETER

Linearity

A linear relationship should be evaluated across the range of the analytical procedure. It was demonstrated directly on the drug substance (by dilution of a standard stock solution) and using the proposed procedure. This method obeys the Beer-Lambert's law in the concentration range of 10-60 µg/ml. (Table No.2and Figure No. 1)

Accuracy

Accuracy was established across the specified range of the analytical procedure. Accuracy is the closeness of the test results obtained by the method to the true value. To study the accuracy 20 tablets were weighed and powdered and analysis of the same was carried out. Recovery studies were carried out by addition of standard drug to the sample at 3 different concentration levels taking into consideration percentage purity of added bulk drug samples. **Table No.3**

Repeatability

Standard solutions of Guaiphenesin (10, 20,30,40,50 and 60 µg/ml) were prepared and a spectrum was recorded. Absorbance was measured at 510nm against blank. The absorbance of the same concentration solution was measured six times and RSD was calculated. The data obtained and results were given in Table No.4 and 5.

Limit of Detection (LOD) & Limit Of Quantization (LOQ)

The limit of detection and quantification of the drugs were calculated with the standard deviation and slope. Table No.6

$$LOD = \frac{3\sigma}{S}$$

$$LOQ = \frac{10\sigma}{S}$$

σ= standard deviation
s= slope of the calibration curve

Reproducibility

Reproducibility is assessed by means of an inter-laboratory trial. The absorbance readings were measured at 510nm at different laboratory using another spectrophotometer and the values obtained were evaluated using % RSD to verify their reproducibility. Table No.7.

Intra and Inter Day Precision

Variation of results within the day (intraday), variation of results between days (inter day) were analyzed. Intraday precision was determined by analyzing Guaiphenesin for three times in the same day at 510 nm. Inter day precision was determined by analyzing the drug different day for three days at 510nm. Table No. 8.

RESULT AND DISCUSSION

Guaiphenesin was estimated based on the reaction of alcoholic solution of 1, 10-phenanthroline in the presence of Ferric chloride. The orange red colour complex formed with ferric chloride and 1, 10-phenanthroline, probably due to oxidation of Guaiphenesin by ferric chloride and thereby itself undergoing reduction from ferric ion to ferrous ion. Further ferrous ion forms a complex with 1, 10-phenanthroline which showed λmax at 510nm. The method obeys Beer-Lambert's law in the concentration ranges of 10-60µg/ml of Guaiphenesin.

CONCLUSION

A method for the determination of Guaiphenesin in bulk and tablet formulation has been developed. It was found that the maximum absorbance at 510nm with ferric chloride. A good linear relationship (0.999) was observed between the concentration ranges of 5-30µg/ml. The proposed makes use of simple reagent, which an ordinary analytical laboratory can afford, so it can be easily used for routine quality control in bulk and tablet dosage form.

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Table 1: Assay Results of Marketed Formulation

Formulation	Actual concentration of Guaiphenesin (µg/ml)	Amount obtained of Guaiphenesin(µg/ml)	% Guaiphenesin
Tablet	10	9.8288	98.288

Table 2: Absorbance of different concentration of Guaiphenesin Obeying beer's law

S.No	Volume of drug taken (100 µg/ml)	Concentration in µg/ml	Absorbance At 510 nm
1	1.0	10	0.1151
2	2.0	20	0.2363
3	3.0	30	0.3443
4	4.0	40	0.4544
5	5.0	50	0.5548
6	6.0	60	0.6734

Table 3: Determination of Accuracy

Amt of sample	Amt. of drug added	Amt. of drug recovered	% Recovery Guaiphenesin µg/ml
20	16	15.8408	99.00
20	20	19.9309	99.65
20	24	23.57953	98.24

Table 4: Repeatability data for Guaiphenesin at 510 nm

Concentration	10 µg/ml	20 µg/ml	30 µg/ml	40 µg/ml	50 µg/ml	60 µg/ml
Absorption	0.1178	0.2342	0.3408	0.4556	0.5521	0.6732
	0.1151	0.2367	0.3384	0.4515	0.5556	0.6765
	0.1164	0.2291	0.3482	0.4602	0.5482	0.6754
	0.1197	0.2408	0.3451	0.4517	0.5611	0.6682
	0.1094	0.2357	0.3505	0.4497	0.5582	0.6728
	0.1127	0.2415	0.3429	0.4582	0.5537	0.6743
Mean.	0.115183	0.23633	0.344317	0.454483	0.554817	0.67340
Std. Dev.	0.003697	0.004561	0.004545	0.004177	0.004559	0.002893
Coefficient variation(RSD)	0.0320	0.01930	0.01320	0.009192	0.00821	0.004296
% RSD	3.20	1.93	0.17	0.91	0.82	0.42

n = 6 determination

Table 5: Repeatability of sample application data for Guaiphenesin

Concentration	Guaiphenesin 10µg/ml
Absorption	0.115
	0.114
	0.115
	0.113
	0.115
	0.114
Mean.	0.114933
Std. Dev.	0.000766
Coefficient variation	0.00666
% RSD	0.66

n = 6 determination

Table 6: LOD AND LOQ

LOD	LOQ
0.034496	0.104561

Table 7: Reproducibility data for Guaiphenesin at 510 nm

Conc. µg/ml	Instrument 1	%RSD	Instrument 2	%RSD	Inference
20	0.234 ± 0.00066	0.28	0.234 ± 0.00056	0.24	Not significant difference

Table 8: Inter and Intraday Precision data for Guaiphenesin at 510 nm

Conc. µg/ml	Inter- day (n=3)	CV	%RSD	Intra- day (n=3)	CV	%RSD
10	0.116±0.000252	0.005608	0.56	0.115 ± 0.000777	0.006752	0.67
20	0.236±0.000404	0.002758	0.27	0.236± 0.000755	0.005497	0.54
30	0.345±0.00030	0.003292	0.32	0.345 ± 0.00070	0.002025	0.20

Table 9: Summary of Parameters of Spectrophotometry

Parameter	Result
λmax(nm)	510 nm
Beer's law limits (µg/ml)	10-60 µg/ml
Molar absorptivity (1/mol.cm)	1.15×10-2
Sandell's equation	0.01722
Regression equation (y=a+bc) Slope (b) Intercept (a)	 b=0.0111 a=0.0057
Correlation coefficient (r2)	0.9995
% Recovery	1) At Level-1 (80%)=99.00 2) At Level-2 (100%)=99.65 3) At Level-3 (120%)=98.24
Repeatability (%RSD)	0.10 to0 .66
Limit of Detection (µg/ml)	0.034496
Limit of Quantization (µg/ml)	0.104561
Specificity	Specific
Selectivity	Selective
Reproducibility (n=6) Instrument 1 (%RSD) Instrument 2 (%RSD)	 0.28 0.24
Precision (n=3) Intraday precision (%RSD) Inter day precision (%RSD)	 0.20-0.67 0.27-0.56

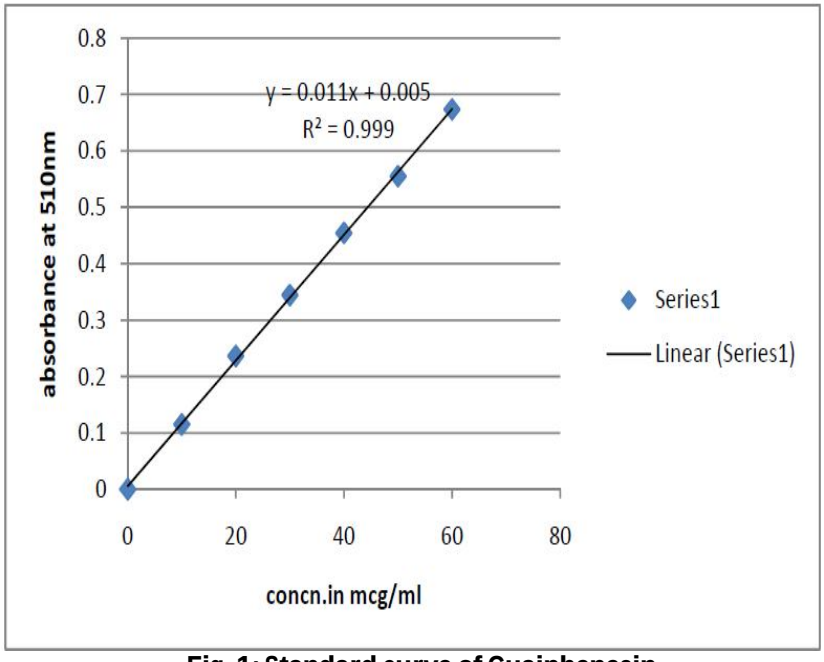

Fig. 1: Standard curve of Guaiphenesin

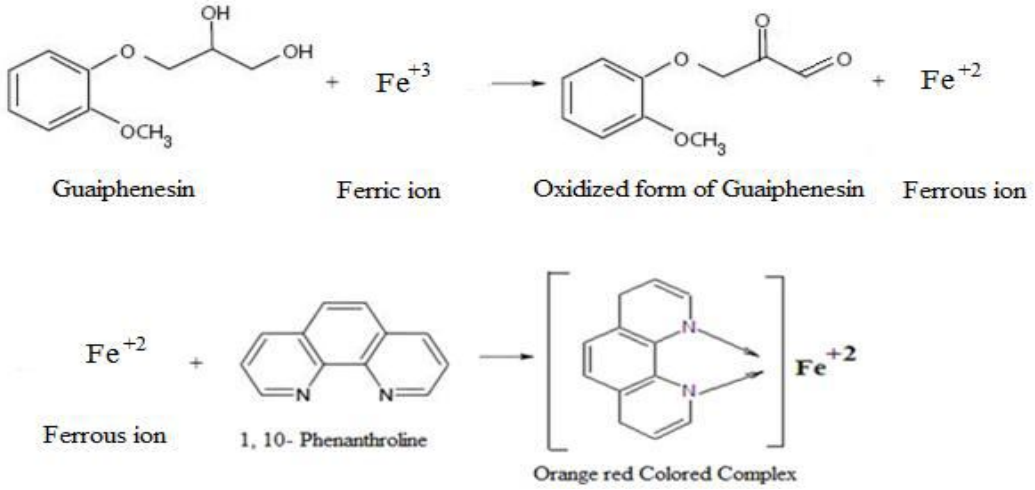

Fig. 2:

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