International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.4, No.3, pp 994-998, July-Sept 2012

Simple Spectrophotometric Methods For Determination Of Ambroxol Hydrochloride From Pharmaceutical Formulation

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Abstract: Simple sensitive and accurate spectrophotometric methods have been developed for the estimation of ambroxol hydrochloride in pharmaceutical dosage form. The drug was diazotised with sodium nitrite in presence of acetic acid and then it was coupled with catechol or resorcinol or β-naphthol in alkaline medium. The resulting coloured chromogenic species in solution were directly measured at their maximum absorption at 425 nm respectively. The proposed methods were validated statistically. The linearity was found to be 1.0-16 µg/ml, 10-60 µg/ml, and 1.0-20 µg/ml for method I, II and III respectively. The low values of standard deviation and percentage RSD indicate high precision of methods. Hence these methods are useful for routine estimation of ambroxol hydrochloride in tablets.
Keywords: Ambroxol Hydrochloride, Glacial acetic acid, Sodium nitrite, Catechol ,Resorcinol,β-naphthol, Sodium hydroxide, Pharmaceutical dosage form.

INTRODUCTION

Ambroxol 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] . Ambroxol 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. A literature survey reveals a spectrophoto - metric[3-6], HPLC[7-12] and miscellaneous[13-19] methods.

MATERIAL AND METHODS

A SHIMADZU -UV1800 double beam uv-visible recording spectrophotometer with pair of 10 mm matched quartz cell was used to measure absorbance of solutions.
A SHIMADZU analytical balance with 0.01 mg was used.

Glacial acetic acid, sodium nitrite, catechol, resorcinol, β-naphthol, resorcinol, and sodium hydroxide of AR grade were used in the study.

Preparation of standard solution and reagents:-
A standard solution of 1000 µg/ ml of ambroxol hydrochloride was prepared by dissolving 100 mg of pure drug in 20 ml alcohol and then diluting the solution to 100 ml with distilled water. Working standard solution of ambroxal hydrochloride of 100 µg /ml concentration was prepared by diluting 10 ml of 1000 µg /ml to 100 ml with distilled water.

A 10% (v/v) solution of acetic acid, 0.5% (w/v) solution sodium nitrite, 0.1% (w/v) of catechol, resorcinol and β-naphthol and 4% (w/v) solution sodium hydroxide were prepared in distilled water.

EXPERIMENTAL

Method I (with Catechol)

Aliquots of the working standard solution of ambroxol hydrochloride (10-160 µg/ml) were transferred in a series of 10 ml volumetric flask. Then 0.5 ml of acetic acid, 2.0 ml of sodium nitrite, 2.0 ml of catechol and 0.3 ml of sodium hydroxide were successively added to each flask and volume was made upto the mark with distilled water. The solutions were allowed to stand for 5 minutes to complete the reaction. The absorbance was measured at 425 nm against reagent blank prepared in similar manner.

Method II (with Resorcinol)

Aliquots of the working standard solution of ambroxol hydrochloride (100-600 µg/ml) were transferred in a series of 10 ml volumetric flask. Then 0.5 ml of acetic acid, 2.0 ml of sodium nitrite and 1.0 ml of resorcinol were successively added to each flask and volume was made upto the mark with distilled water. The solutions were allowed to stand for 5 minutes to complete the reaction. The absorbance was measured at 425 nm against reagent blank prepared in similar manner.

Method III (with β-naphthol) Aliquots of the working standard solution of ambroxol hydrochloride (10-200 µg/ml) were transferred in a series of 10 ml volumetric flask. Then 0.5 ml of acetic acid, 1.5 ml of sodium nitrite, 0.6 ml of β-naphthol and 1.0 ml of sodium hydroxide were successively added to each flask and volume was made upto the mark with distilled water. The solutions were allowed to stand for 5 minutes to complete the reaction. The absorbance was measured at 425 nm against reagent blank prepared in similar manner.

Estimation from tablets

Twenty tablets of labelled claim 30 mg of ambroxol hydrochloride were weighed accurately. Average weight of each tablet was determined. Tablets were crushed into fine powder. An accurately weighed quantity of powder equivalent to 100 mg of ambroxol hydrochloride was transferred into a beaker and it was shaken with 20 ml of ethyl alcohol and filtered. The filtrate and the washing were collected in a 100 ml volumetric flask. This filtrate and the washing were diluted up to the mark with distilled water to obtain concentration as 1000 µg /ml. A 10 ml of 1000 µg /ml solution was further diluted to 100 ml with distilled water to give final concentration of 100 µg/ml.

Appropriate aliquots of drug solution were taken. The individual assay procedures was carried out for the estimation of drug contents in tablets. The concentration of the drug in the tablets was calculated using calibration curve. The recovery experiment was carried out by standard addition method. The values of optical and regression terms of analysis are given **in table no I.**

Table I : Optical and regression of drug in different methods

Parameter	Methods		
	I	II	III
λ max (nm)	425	425	425
Beer Law Limits (µg/ml)	1-16	10-60	1-20
Molar absorptivity(L/mol.cm)			
Sandell's sensitivity			
Correlation coefficient(r^2)	0.999	0.9999	0.999
Regression equation (y=b+ac)			
Slope (a)	0.060	0.009	0.045
Intercept	-0.002	-0.002	-0.002

Table II : Results of recovery of drug for Catechol.
Method I

Amount of drug added µg/ml	Amount of standard added µg/ml.	Total amount recovered	Percent recovery (%)	Standard deviation	Percentage of relative standard deviation C.O.V.	Mean standard deviation	Mean of C.O.V.
1	0	1.0214	102.14	0.04243	4.1539		
2	1	2.0000	100.00	0.06801	3.4007	0.05771	2.7570
3	2	3.0119	100.39	0.05748	1.9085		
4	3	4.0238	100.59	0.06297	1.5649		
Mean of percent (%) recovery = 100.78							

Table III : Results of recovery of drug for Resorcinol
Method II

Amount of drug added µg/ml	Amount of standard added µg/ml.	Total amount recovered	Percent recovery (%)	Standard deviation	Percentage of relative standard deviation C.O.V.	Mean standard deviation	Mean of C.O.V.
10	0	10.1429	101.429	0.28305	2.79064		
20	10	20.1587	100.794	0.41999	2.08343	0.41630	1.9035
30	20	30.1587	100.529	0.41999	1.39260		
40	30	40.2381	100.595	0.54218	1.34744		
Mean of percent (%) recovery = 100.586							

Table-IV : Results of recovery of drug for β-naphthol
Method III

Amount of drug added µg/ml	Amount of standard added µg/ml.	Total amount recovered	Percent recovery (%)	Standard deviation	Percentage of relative standard deviation C.O.V.	Mean standard deviation	Mean of C.O.V.
1	0	1.0159	101.59	0.07667	7.54663		
2	1	2.0000	100.00	0.09071	4.53563	0.08018	4.1333
3	2	3.0159	100.53	0.07667	2.54207		
4	3	4.0159	100.398	0.07667	1.90906		
Mean of percent (%) recovery = 100.629							

RESULT AND DISCUSSION

The spectrophotometric methods are popular due to their sensitivity in assay of the drug and hence spectrophotometric methods have gain considerable attention for quantitative determination of many pharmaceutical preparations. These proposed methods are spectrophotometric methods for the determination of ambroxol hydrochloride from its formulations i.e. tablets.

The colour chromogens are formed and are stable. The working conditions of these methods were established by varying one parameter at time and keeping the other parameters fixed by observing the effect produced on the absorbance of the colour species. The various parameters involved for maximum colour development for these methods were optimized. The proposed methods were validated statistically and by recovery studies. The molar absorptivity and Sandell's sensitivity values (Table no. I) show the sensitivity of methods while the precision was confirmed by % RSD (relative standard deviation). The optical characteristics such as absorption maxima (nm), molar absorptivity (L $mole^{-1}$ cm^{-1}), correlation coefficient (r) and sandell sensitivity ($\mu g/cm^2/0.001$) were calculated and are also summarized in table I. Assay results of recovery studies are given in table no. II, III and IV.

Results are in good in agreement with labelled value. The percent recovery obtained indicates non interference from the common excipient used in the formulation. The reproducibility, repeatability and accuracy of these methods were found to be good, which is evidenced by low values of standard deviations.

The proposed methods suggested in literature were applied need costly reagent for development of chromogen and useful in higher concentration. The proposed methods are simple, sensitive, accurate, precise, and reproducible applicable to even very low concentration as compare to previous methods suggested in literature. They are directly applied to drug to form chromogen. Hence they can be successfully applied for the routine estimation of ambroxol hydrochloride in bulk and pharmaceutical dosage form even at very low concentration in formulation such as tablets.

The strong recommendation is made here for the proposed methods for determination of ambroxol hydrochloride from its formulation viz. tablets.

ACKNOELEDGEMENT

Authors express sincere thanks to the Principal Dr. T.M. Desai of D. G. Ruparel college for providing necessary facilities work , Dr.Atul Pusalkar for providing gift sample of ambroxol hydrochloride.

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