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SIMULTANEOUS ESTIMATION OF PHENYLPROPANOLAMINE HYDROCHLORIDE AND TRIPROLIDINE HYDROCHLORIDE IN PHARMACEUTICAL PREPERATIONS BY RP- HPLC METHOD

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ABSTRACT

A simple and precise reversed phase HPLC method was developed for the stimulation estimation of phenylpropanolamine and triprolidine in tablet formulation. The method was carried out on a shimpack C_8 (25 cm x 4.6mm i.d., 5µ) column with a mobile phase consisting of Acetonitrile: phosphate buffer (25mM) of pH 3.0 (35:65v/v) at a flow rate of 1.2ml/min.detection was carried out at 210 nm. The guaiphenesin was used as an internal standard. The retention time of phenylpropanolamine, triprolidine and guaiphenesin was 2.58, 6.53, and 3.84min respectively. The validation of propped method is specific, accurate, precise and linear. The linearity and range of phenylpropanolamine and triprolidine was to 5 to 15 µg/ml and 50 to 150µg/ml, respectively. The proposed method can be used for simulatious estimation of phenylpropanolamine and triprolidine in tablet formulation by HPLC method.

Keywords: phenylpropanolamine; triprolidine; simultaneous estimation

1. INTRODUCTION

Phenylpropanolamine hydrochloride, chemically (1RS, 2SR)-2-amino-1–phenylpropan-1-ol-hydrochloride, is used for the symptomatic treatment of nasal congestion. It is official in British Pharmacopoeia, Indian Pharmacopeias and United State Pharmacoepia [1- 3.]. Triprolidine hydrochloride, chemically (ε) -2-(3-pyrolidine-1-yl-1(4-toly)prop-1-enyl-pyridine hydrochloride monohydrate), used as antihistamine with central sedative & antimuscrinic effect, for the symptomatic relief of hypersensitivity reaction including urticaria, skin disorders. It is official in British Pharmacopoeia, Indian Pharmacopoeia & United States Pharmacopoeia [1- 3.]

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A combination of 25 mg of Diphenhydramine hydrochloride and 2.5 mg triprolidine is available commercially as tablets and used for the various etiologies.

Many methods have been described in the literature for the determination of phenylpropanolamine and triprolidine, individually and with other drugs [4-14]. However, there is no HPLC method for the simultaneous estimation of phenylpropanolamine and triprolidine in combined dosage forms. The present work describes a simple, precise and accurate reversed phase HPLC method for the simultaneous estimation of phenylpropanolamine and triprolidine in combined dosage forms.

2. MATERIALS AND METHODS

2.1 Reagent And Chemicals

Acetonitrile HPLC grade were supplied by Qualigens Chemicals, Mumbai. Orthophosphoric acid AR grade and Sodium

dihydrogen orthophosphate AR grade were supplied by S.D.fine chemicals Ltd, Mumbai. Water HPLC grade was obtained from Milli-Q RO system. Reference drugs were obtained as gift samples from Tablets India Ltd, Chennai, INDIA

2.2 Chromatographic Conditions

A WATERS® HPLC system was used for analysis. The method was carried out on a Shimpac ®$C_{18,}$ (25 cm x 4.6 mm i.d., 5 µ) column with a mobile phase consisting of Acetonitrile: Phosphate buffer (25mM) of pH 3.0 (65: 35 v/v) at a flow rate of 1.2 ml min^{-1} a Rheodyne ® 7125 injector with a 20 µl loop was used for the injection of samples. The WATERS® 486 tunable absorbance detector was used to detect the drugs at 210 nm of the standard drug solution(10 mg/ml) were scanned, individually in the UV Range of 200-400nm using Shimadzu UV 1700 Spectrophotometer, and from over lapping spectra the wavelength of 210 nm was selected with a sensitivity of 0.20 AUFS. The mobile phase was filtered through a 0.45 µ membrane filter and degassed. The separation was carried about at room temperature of about 20±2° C.

Preparation Of Standard Solution

Standard Stock solution is prepared by adding of 1 mg/ml of phenylpropanolamine, Triprolidine and Guaiphenesin (as internal standard) were taken into 100 ml standard volumetric flask separately using a mixture of water and Acetonitrile (1:1 v/v) and mixed it vigorously. From the standard stock solutions, mixed standard solution was prepared to contain 100 µg /ml of phenylpropanolamine, 10 µg /ml Triprolidine and 50 µg /ml Guaiphenesin(as internal standard).

2.3 Preparation of Sample Solution

Twenty tablets, each containing 25 mg of Phenylpropanolamine and 2.5 mg of Triprolidine were weighed and collect the powder, weight a quantity of powder equivalent to 100 mg of Phenylpropanolamine and 10 mg of Triprolidine transferred to a sintered glass crucible and to this add 50 mg of Guaiphenesin as internal standard, extract with mixture of Acetonitrile and water (1:1 v/v) for 3 times (3x25 ml) combine the extracts and makeup volume to 100 ml with mobile phase and filter. Resulting solution was further diluted to get a concentration 100 µg/ml of Phenylpropanolamine and 10µg/ml of Triprolidine 50 µg/ml of Guaiphenesin 20 µg/ml of Domperidone , 40 µg/ml of Omeprazole and 20 µg/ ml of paracetamol (as internal standard) (theoretical value) and this was used for the estimation (sample solution).

2.4 Procedure

With the above optimized chromatographic conditions, the standard solution and sample solution containing internal standard were injected and the chromatograms were recorded. The retention times of phenylpropanolamine, Triprolidine and Guaiphenesin were found to be 2.58, 6.53 and 3.84 minutes, respectively. The response factor (peak area ratio of standard peak area and the internal standard peak area) of the standard solution and the sample solution were calculated.

The concentration of the drugs were calculated using the following formula-

$$\text{Concentration Of Drug} = \frac{\text{Response Factor of the Sample}}{\text{Response Factor of the Standard}} \times \text{Concentration of Standard}$$

2.5 Validation of the method

Accuracy of method was studied by the recovery experiments. To the powdered tablet formulations (each containing 25 mg of Phenylpropanolamine and 2.5 mg of Triprolidine) the reference standard drugs were added at the level of 25% to 50% of

the label claim. The extraction off drugs was followed using sample preparation procedure and these were analyzed. The percentage recovery was calculated and presented (Table-1).

The precision of the method was by repeatability studies. The percentage recovery was demonstrated by the standard solution for 10 times and passing them through the assay procedure.

Linearity and Range of the method was done by analyzing mixed standard solution containing 50 to 150 % of the targeted level of the assay concentration 50 to 150 µg/ml of phenylpropanolamine and 5 to 15 µg/ml Triprolidine respectively. These were analyzed and the response factors were calculated. The calibration curve was plotted using response factor Vs concentration of the standard solutions.

The limit of Detection (LOD) and limit of Quantification (LOQ) of the method was determined by injecting progressively low concentrations of the standard solutions. The system suitability studies were also carried out and the parameters like column efficiency, resolution and peak asymmetry were calculated.

Table 1:- Analysis of formulation and recovery studies

Drug	Labeled amount (mg/tab)	Amount taken (µg/ml)	Amount obtained (µg/ml)*	% Label Claim	% Recovery
Phenylpropanolamine	25	100	99.55± 0.490	99.55± 2.49	99.98± 0.124
Triporlidine	25	100	9.74± 0.4368	97±3.368	99.87± 0.299

*Mean± SD of 6 observations

Table 2:- Linearity and Range

Internal Standard Peak Area	Phenylpropanolamine		Triprolidine	
	Conc. (µg/ml)	Peak Area	Conc. (µg/ml)	Peak Area
2750398	5	320879	50	716459
	7.5	481317	75	1074694
	10	641772	100	1432926
	12.5	802217	125	1791149
	15	962651	150	2149389

Table 3:- System Suitability

S.No.	Parameters	Phenylpropanolamine	Triprolidine	Guaiphenesin
1	Theoritical plates	1164	6155	10113
2	Resolution	-	4.02	4.63
3	Asymmetry (10%)	1.02	1.01	1.05
4	Capacity factor	0.30	1.50	3.30
5	LOD(ng/ml)	5	10	10
6	LOQ(ng/Mml)	25	50	50

Fig 1:- Phenylpropranolamine linearity curve

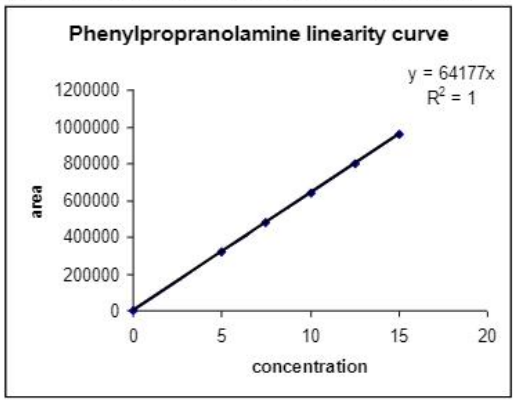
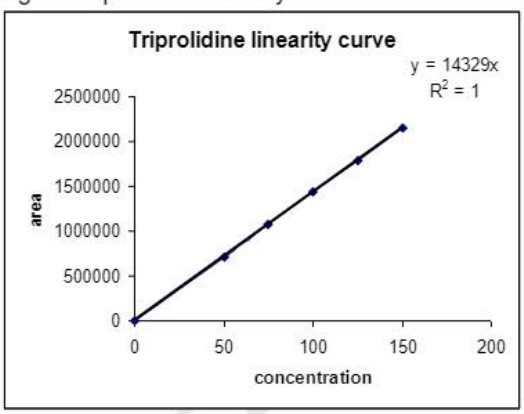


Fig 2:- Triprolidine linearity curve



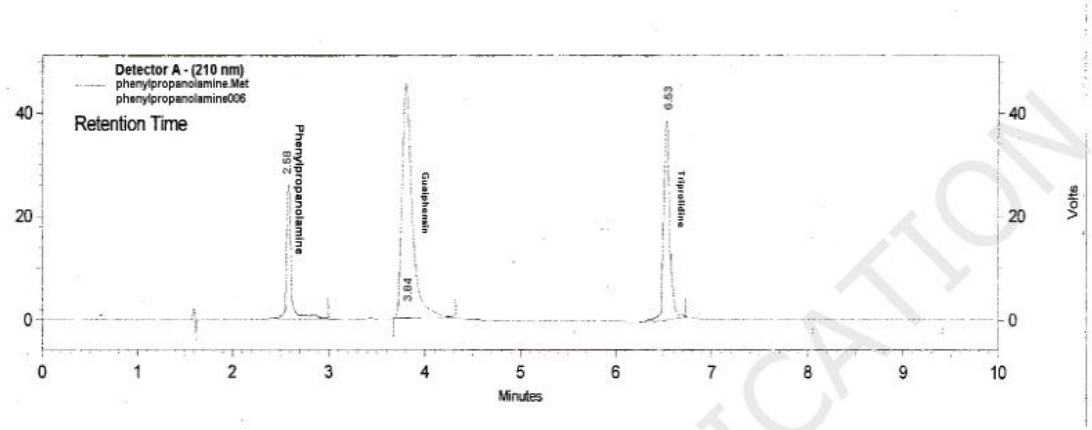
RESULTS AND DISCUSSIONS

The chromatogram of mixed standard solution and sample solution were recorded. The accuracy of the method was determined by the recovery studies. The recovery studies were carried out and the percentage was calculated from the data obtained, recoveries for the standard drugs were considered sufficiently accurate. The precision data shows that the reproducibility of the assay procedure was satisfactory. The concentration range from 5 to 15 µg/ml of phenylpropanolamine and 50 to 150 µg/ml of triprolidine was examined by the assay procedure and the calibration curves were plotted. The calibration curve shows linear response over the range of concentration used in the assay procedure. The calibration curve passes through the origin, which justifies the use of single point calibration and the proximity of all points to the calibration line demonstrated that the method has adequate linearity to the concentration of the analyte. The limit of detection (LOD) for phenylpropanolamine, triprolidine and guaiphenesin was found to be 5ng/ml, 10ng/ml and 10ng/ml respectively and the limit of quantification (LOQ) was 25ng/ml, 50ng/ml and 50ng/ml for phenylpropanolamine, triprolidine and guaiphenesin. The ruggedness of the method was determined by carrying out the experiments on different instruments like Spectraphysics HPLC system(SP 8810), Shimadzu HPLC(LC-10AT VP) and WATERS gradient HPLC by different operators using different columns of similarity like Kromasil C_{18} , Kromasil C_{8}, Hypersil C_{18} Bondapak C_{18}. Robustness of the method was determined by making slight changes in the chromatographic conditions. The ruggedness and robustness of the method showed that there were no marked changes in the chromatographic parameters, which demonstrated that the method developed is rugged and robust. Further there is no interface due to excipients. The system suitability studies were also carried out to determine column efficiency, resolution and peak asymmetry.

CONCLUSION

The proposed HPLC method is simple, accurate, precise, linear and rapid. Hence this method is suitable for the quality control of raw materials, formulations and can be applied in dissolution studies.

Fig 3:- HPLC Chromatogram



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