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Journal of Pharmaceutical and Biomedical Analysis
24 (2000) 25–31

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

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Simultaneous estimation of phenylpropanolamine HCl, guaiphenesin and diphenylpyraline HCl in syrups by LC

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Received 31 January 2000; received in revised form 2 May 2000; accepted 27 May 2000

Abstract

A simple, precise and accurate HPLC method was developed for the simultaneous estimation of phenylpropanolamine HCl, guaiphenesin and diphenylpyraline HCl in syrup. The method was carried out on a Shimpak® C_8 column with a mobile phase consisting of acetonitrile-triethylamine (pH adjusted to 3.5 using orthophosphoric acid; 0.5%), (35:65, v/v) at a flow rate of 1.2 ml min^{-1}. Detection was carried out at 210 nm. Diphenhydramine was used as internal standard. The validation of the method was also carried out.

Keywords: Phenylpropanolamine HCl; Guaiphenesin; Diphenylpyraline HCl; Simultaneous estimation; Syrup; Reversed phase chromatography

1. Introduction

Phenylpropanolamine HCl is chemically, (±)-α-(1-aminoethyl) benzene methanol hydrochloride and is decongestant, anorexic. Guaiphenesin is chemically, (RS)-3-(2-methoxyphenoxy) propane-1,2-diol and is used for the symptomatic relief of respiratory conditions. Diphenylpyraline HCl is chemically, 4-benzohydryloxy-1-mehtyl piperidine hydrochloride and is histamine H_1 receptor antagonist. The combination of these three drugs is commercially available as syrup. The 5 ml of syrup contains 10 mg of phenylpropanolamine HCl, 50 mg of guaiphenesin and 1.5 mg of diphenylpyraline HCl, which is used in the treatment of cold and cough associated with nasal allergy, rhinitis, influenza, sinusitis and bronchitis.

Many methods have been reported in the literature for the estimation of phenylpropanolamine HCl, guaiphenesin and diphenylpyraline HCl individually and in combination with other drugs [1–9]. However, there is no method reported for the simultaneous estimation, Hence the present work describes a simple, precise, and accurate method for simultaneous estimation of these three drugs in syrup. The validation of the proposed method was also carried out [10].

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0731-7085/00/$ - see front matter
PII: S0731-7085(00)00385-X

2. Experimental

2.1. Reagents and chemicals

Triethylamine AR grade, orthophosphoric acid AR grade and acetonitrile of HPLC grade supplied by S.D. Fine Chemicals, Water HPLC grade obtained from Milli-Q RO system, were used. Reference Standards of Phenylpropanolamine HCl, Guaiphenesin and Diphenylpyraline HCl were obtained as gift samples.

2.2. Chromatographic conditions

A Shimadzu® HPLC system was used for the analysis. The method was carried out on a Shimpak® C_8 (25 cm × 4.6 mm i.d., 10 μ) column as a stationary phase and acetonitrile-triethylamine (pH adjusted to 3.5 using orthophosphoric acid; 0.5%) (35:65, v/v) as mobile phase at a flow rate of 1.2 ml min^{-1}. A Rheodyne 7725*i* injector with a 20 μl loop was used for the injection of samples. The SPD-M10Avp Photodiode array detector was used to detect the drugs at 210 nm and CLASS VP data station was used to process the chromatograms. The mobile phase was filtered through a 0.45 μ membrane filter and degassed. The separation was carried out at room temperature of about 20°C.

2.3. Preparation of solutions

Standard stock solution of 1mg ml^{-1} of phenylpropanolamine HCl, guaiphenesin, diphenylpyraline HCl and diphenhydramine were prepared, separately using a mixture of water–acetonitrile (1:1, v/v). From the standard stock solutions, mixed standard solution was prepared using the mobile phase to contain 20 μg ml^{-1} of phenylpropanolamine HCl, 100 μg ml^{-1} of guaiphenesin, 3 μg ml^{-1} of diphenylpyraline HCl and 25 μg ml^{-1} of diphenhydramine as internal standard (standard solution).

Five ml of the syrup was taken into a 100 ml standard flask. To this 25ml of 1mg ml^{-1} of diphenhydramine was added, vortexed for 15 min and made up to 100 ml with mobile phase. The resulting solution was further diluted using the mobile phase to get a concentration of 20 μg ml^{-1} of phenylpropanolamine HCl, 100 μg ml^{-1} of guaiphenesin, 3 μg ml^{-1} of diphenylpyraline HCl and 25 μg ml^{-1} of diphenhydramine (theoretical value) and this was used for the estimation (sample solution).

2.4. Procedure

With the above chromatographic conditions, the standard solution and sample solution were injected and the chromatograms were recorded (Fig. 1). The retention time of phenylpropanolamine HCl, guaiphenesin, diphenylpyraline HCl and diphenhydramine, were found to be 2.17, 3.56, 7.37 and 5.79 min, respectively. The response factor of the standard solution (peak area ratio of standard peak area and the internal standard peak area) and the sample solution were calculated. The concentrations of the drugs were calculated using the following formula.

$$\text{Concentration of drug} = \frac{\text{Response factor of the sample}}{\text{Response factor of the standard}} \times \text{Concentration of standard}$$

3. Validation of the method

The specificity of the method was carried out by peak purity test method using the diode array detector. The Diode array first derivative spectrum were recorded for the sample peaks and these were compared with the first derivative spectrum of standard drug peaks.

Accuracy of the method was studied by recovery experiments. Five ml of the syrup formulations was taken in 100 ml standard flask. To this 25 ml of 1 mg ml^{-1} of diphenhydramine solution, the standard drugs at the level of 25.0 and 50.0% of the label claim, respectively were added and made upto 100 ml with the mobile phase. The further dilutions of these solutions were followed using the sample preparation procedure. The resulting solutions were analysed and the percentage recoveries were calculated.

Precision of the method was demonstrated by repeatability studies. This was done by injecting consecutively the standard solution for 10 times and passing them through the assay procedure. The response factor of the drug peaks, mean and percentage RSD of the response factor of the peaks were calculated.

Linearity and range of the method was done by analysing mixed standard solution containing 10–30 μg ml^{-1} of phenylpropanolamine HCl, 50–150 μg ml^{-1} of guaiphenesin and 1.5–4.5 μg ml^{-1} of diphenylpyraline HCl (50 to 150% of targeted level of the assay concentration) containing 25 μg ml^{-1} of diphenhydramine as internal standard, respectively. These were analysed 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.

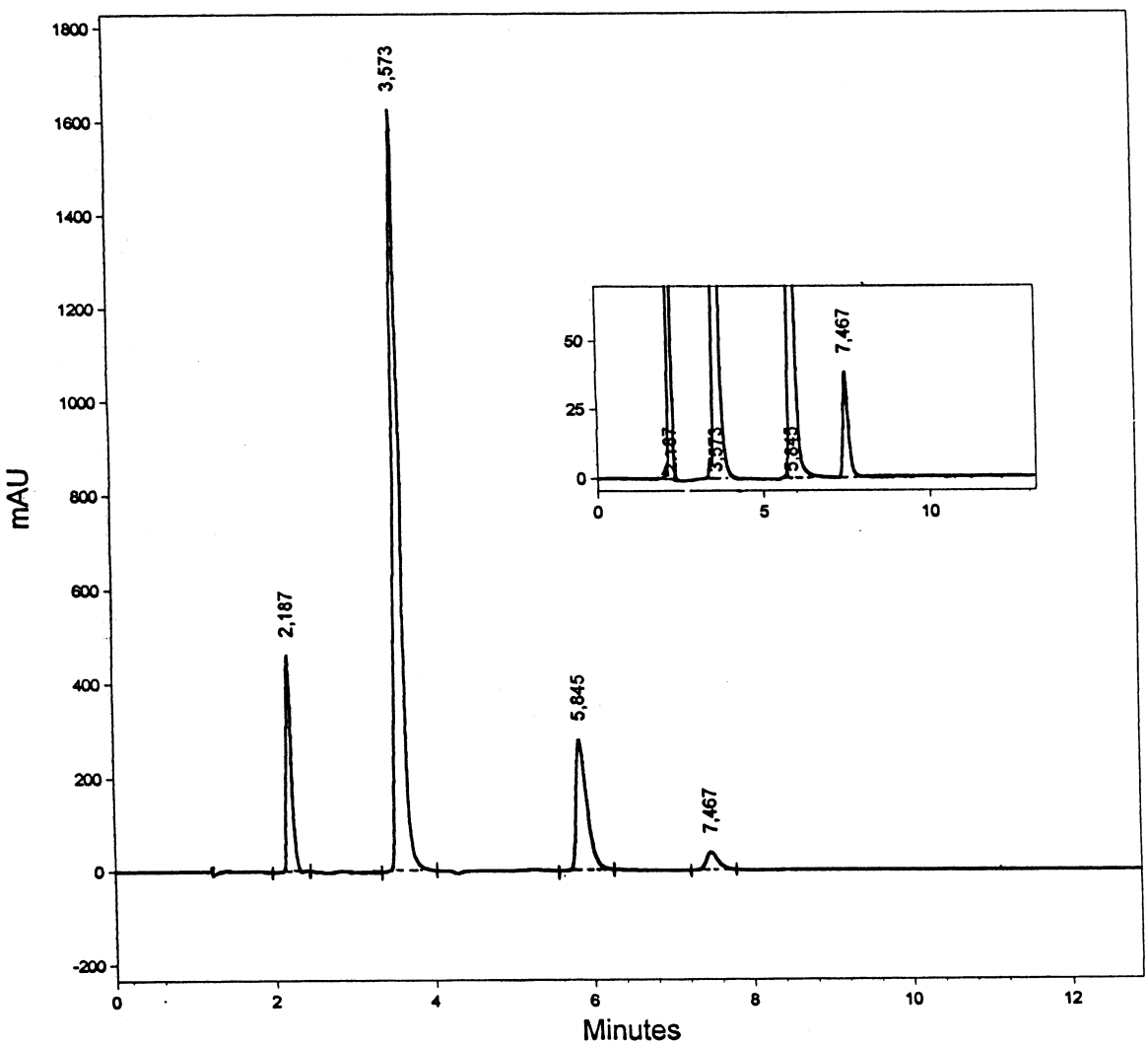

Fig. 1. Phenylpropanolamine HCl, guaiphenesin and diphenylpyraline HCl in syrup solution.

Table 1
Analysis of formulation and recovery studies

Drug	Labelled amount (mg/5 ml syrup)	Amount taken for assay (μg/ml)	Amount Obtained[a] (mg/5 ml syrup)	% Label claim[a]	% Recovery[a]
Phenylpropanolamine HCl	10	20	19.96 ± 0.2042	99.8 ± 1.021	100.4 ± 1.019
Guaiphenesin	50	100	100.7 ± 1.124	100.7 ± 1.124	99.5 ± 1.165
Diphenylpyraline HCl	1.5	3	3.012 ± 0.065	100.4 ± 2.014	101.2 ± 1.425

[a] Mean ± SD of 6 observations.

The ruggedness of the method was carrying out by changing the experimental conditions such as, changing the source of reagents and solvents (different manufacturers), changing to another stationary phase of similar type (Kromasil C_8 and Zorbax C_8) and using other branded HPLC instruments (Waters HPLC and Spectraphysics HPLC) and the chromatographic pattern were studied.

Stability of the analytes, mobile phase, standard and sample solutions were subjected to long term (3 days) stability studies. The stability of these solutions was studied by performing the experiment and looking for the change in the chromatographic pattern compared with freshly prepared solutions.

The system suitability studies were also carried out and the parameters like column efficiency, resolution and peak asymmetry were calculated.

4. Results and discussion

The results of the proposed HPLC method showed that the results are consistent with the label claim of the formulation (Table 1). The specificity of the method was carried out by peak purity tests using diode array detector and the first derivative spectrum of standard and sample peaks were recorded. The first derivative spectrum of the sample peaks were matching with the corresponding first derivative spectrum of the standard drug peaks, which shows that the peaks of analyte were pure and also formulation excipients and impurities were not interfering with the analyte peaks. The accuracy of the method was determined by recovery studies. The recovery studies were carried out and the percentage recovery was calculated (Table 1). From the data obtained, recoveries of the standard drugs were accurate. The percentage RSD values for the Phenylpropanolamine, Guaiphenesin and Diphenylpyraline were found to be 0.8065, 0.2597 and 0.2320. This percentage RSD value shows that the method is precise. The linearity and range of the assay method was done and the calibration curves were plotted (Table 2). The calibration curve showed linear response over the range of concentration used in the assay procedure, which justifies the use of single point calibration. The slope and intercept of the regression equations were found to be 28.239, −0.0211 for phenylpropanolamine, 29.227, −0.0002 for guaiphenesin and 18.305, 0.0134 for diphenylpyraline, respectively. The percentage RSD values were 0.976, 0.667 and 0.413 for phenylpropanolamine, guaiphenesin and diphenylpyraline, respectively. The LOD for phenylpropanolamine HCl, guaiphenesin, diphenylpyraline HCl and diphenhydramine was found to be 10, 25, 25 and 25 ng ml^{-1}, respectively and the LOQ was 25, 50, 50 and 50 ng ml^{-1} for phenylpropanolamine HCl, guaiphenesin, diphenylpyraline HCl and diphenhydramine (Table 3). The ruggedness of the method was studied and it was observed that there were no significant changes in the chromatographic pattern when slight changes were made in experimental condition showed that the method is rugged. The stability of the solutions were studied and the data obtained showed that the mobile phase, sample and standard solutions were stable up to three days when these were stored at about 5°C (in refrigerator). The system suitability studies were

Table 2
Linearity and range

Internal standard	Phenylpropanolamine HCl			Guaiphenesin			Diphenylpyraline HCl		
Peak area (25 μg ml^{-1})	Concentration (μg ml^{-1})	Peak area	Response factor	Concentration (μg ml^{-1})	Peak area	Response factor	Concentration (μg ml^{-1})	Peak area	Response factor
1 479 731	10	52 4458	0.3564	50	2 531 117	1.7105	1.50	120624	0.0815
	15	78 6740	0.5323	75	3 796 654	2.5657	2.25	180938	0.1224
	20	1 048 939	0.7088	100	5 062 218	3.4210	3.00	241243	0.1645
	25	1 311 189	0.8861	125	6 327 765	4.2762	3.75	301562	0.2041
	30	1 573 409	1.0633	150	7 593 317	5.1315	4.50	361859	0.2453

also carried out to determine column efficiency, resolution and peak asymmetry (Table 3). The 3D chromatogram of the sample solution showed that there is no interference due to formulation excipients (Fig. 2). The developed HPLC method is simple, accurate, precise, linear and rapid. Hence this method is suitable for the quality control of raw materials and formulation.

Acknowledgements

The authors are thankful to His Holiness Jagadguru Sri Sri Shivarathri Deshikendra Mahaswamigalavaru of Sri Suttur Mutt and Dr B. Suresh, Principal, J.S.S. College of Pharmacy, Ootacamund for providing facilities for research work.

Table 3
System suitability studies

S. No.	Parameters	Phenylpropanolamine HCl	Guaiphenesin	Diphenhydramine	Diphenylpyraline HCl
1	Theoretical plates	4343	13 079	13 241	13 301
2	Resolution factor	–	6.00	7.46	3.89
3	Asymmetric factor	1.00	1.01	1.01	1.01
4	LOD (ng/ml)	10	25	25	25
5	LOQ (ng/ml)	25	50	50	50

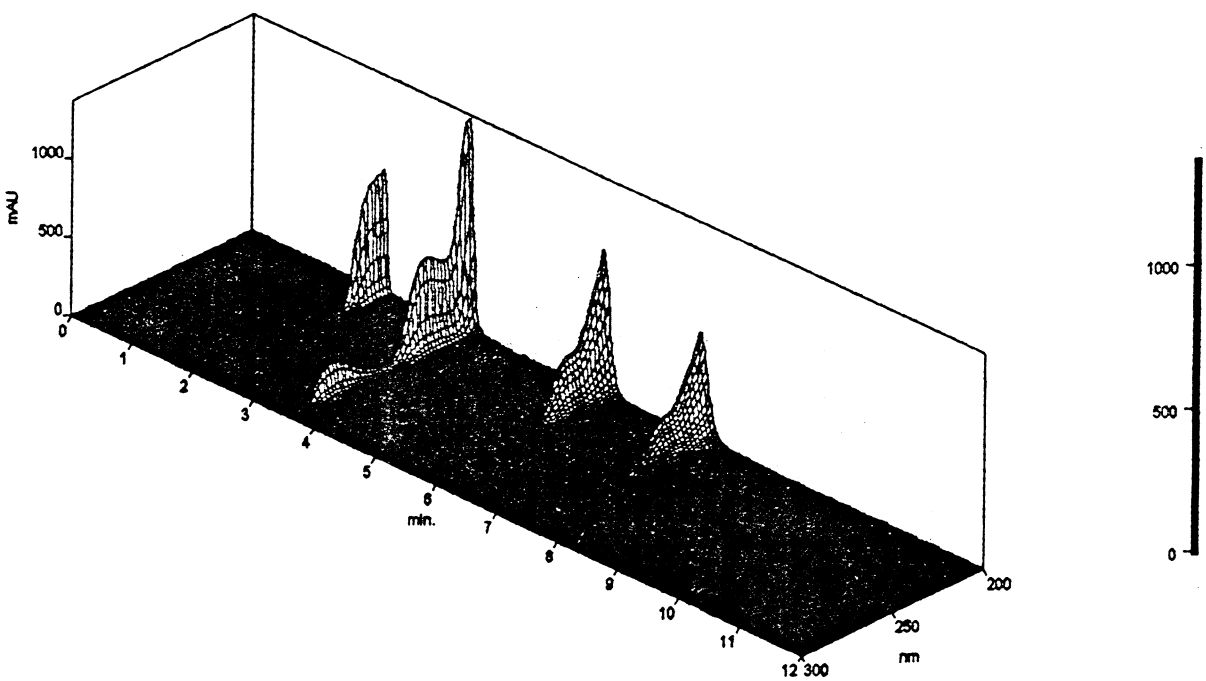

Fig. 2. 3D chromatogram of phenylpropanolamine HCl, guaiphenesin and diphenylpyraline HCl in syrup solution.

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