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A NOVEL HPLC METHOD FOR THE SIMULTANEOUS DETERMINATION OF CHLORPHENIRAMINE MALEATE AND DEXTROMETHORPHAN IN BULK AND PHARMACEUTICAL FORMULATION

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ABSTRACT: Chlorpheniramine maleate and Dextromethorphan are used in treatment of cough caused by allergies and the common cold by decreasing intra ocular pressure. The present study was designed to develop and validate a simple, sensitive, precise and accurate reverse phase high performance liquid chromatographic (HPLC) method for simultaneous determination of Chlorpheniramine maleate and Dextromethorphan in tablet dosage form. Chromatographic separation of these two drugs was achieved on Discovery C18 column (250 x 4.6 mm, 5 µm) as stationary phase with a mobile phase of Water (pH 2 adjusted with OPA): Acetonitrile (60:40v/v) at a flow rate of 1 ml/min and PDA detection at 218 nm. The retention times of Chlorpheniramine maleate and Dextromethorphan were found to be 3.0 min and 3.6 min respectively. The proposed method was validated for system suitability, linearity, accuracy, precision, LOD, LOQ and robustness. The calibration curves were linear in the concentration range of 50% to 150% of the working concentration ($r^2 = 0.999$) for both the drugs in binary mixture. The LOD was found to be 0.04 µg/ml and 0.11 µg/ml and LOQ was found to be 0.14 µg/ml and 0.43 µg/ml for Chlorpheniramine maleate and Dextromethorphan respectively. Hence the proposed RP-HPLC method can be used in routine analysis of tablets containing Chlorpheniramine maleate and Dextromethorphan.

INTRODUCTION: Chlorpheniramine maleate is chemically 2-[p-Chloro - a - [2-(dimethylamino) ethyl] benzyl] pyridine maleate, is a histamine H1 antagonist used in allergic reactions, hay fever, rhinitis, urticaria, and asthma. Dextromethorphan is chemically (4*bS*, 8*aR*, 9*S*) -3- Methoxy-11-methyl-6,7,8,8*a*,9,10-hexahydro-5*H*-9,4*b*-(epiminoethano) phenanthrene, is an N-methyl-D-aspartate receptor antagonist used as cough suppressant.

Extensive literature survey revealed that there were analytical methods for the estimation of specified drugs with other combinations¹⁻¹⁴. There was no method has been reported for the simultaneous estimation of Chlorpheniramine maleate and Dextromethorphan. Hence we presented a simple analytical method for simultaneous determination of Chlorpheniramine maleate and Dextromethorphan in bulk and pharmaceutical preparation.

MATERIALS AND METHODS:

Materials: Chlorpheniramine maleate and Dextromethorphan were obtained from Spectrum Labs, Hyderabad. Cheston meltees tablets were taken for study which contain 2 mg Chlorpheniramine maleate and 10 mg Dextromethorphan. Acetonitrile, Ortho phosphoric

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acid (OPA) and HPLC grade water were used of analytical grade from Merck.

Diluent: Water: Acetonitrile has taken in the ratio 50:50 % v/v.

Standard stock solution preparation: 2 mg of Chlorpheniramine maleate and 10 mg of Dextromethorphan standards were accurately weighed and transferred into a 10 ml clean dry volumetric flask, 5 ml of diluent was added, sonicated for 5 minutes and made up to the final volume with diluent. Further 1ml from the above stock solution was taken into a 10ml volumetric flask and made up to 10ml with diluent.

Sample solution preparation: 20 tablets were weighed and crushed. A powder equivalent to 2 mg of Chlorpheniramine maleate and 10 mg of Dextromethorphan was taken and then transferred into a 10 ml clean dry volumetric flask, 5 ml of diluent was added, sonicated for 5 minutes and made up to the final volume with diluent. Further 1 ml from the above stock solution was taken into a 10 ml volumetric flask and made up to 10 ml with diluent.

Chromatographic Conditions: The criteria employed for selecting the mobile phase for the analysis of the drugs were cost involved, time required for the analysis and better separation of drugs. Chromatographic separation was performed on reverse phase Waters Discovery C18 (250 x 4.6 mm, 5 μ) column. The mobile phase consisted of water (pH 2 adjusted with OPA): acetonitrile (60:40v/v) with PDA detection at 218 nm. The flow rate was set at 1.0 ml/min for simultaneous determination of Chlorpheniramine maleate and Dextromethorphan.

Method Development: Different chromatographic conditions were tried for separation and resolution. Waters symmetry Discovery column was found satisfactory. Peak purity of Chlorpheniramine maleate and Dextromethorphan was checked using photo diode array detector and 218 nm was considered satisfactory for detecting both the drugs with adequate sensitivity. A typical RP-HPLC chromatogram for simultaneous determination of Chlorpheniramine maleate and Dextromethorphan from standard preparation and from pharmaceutical formulation was shown in **Fig. 1** and **2**.

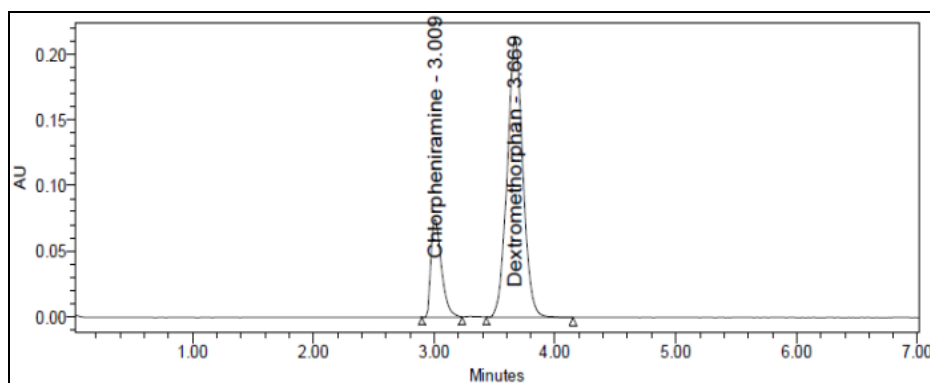


FIG. 1: CHROMATOGRAM OF CHLORPHENIRAMINE MALEATE AND DEXTROMETHORPHAN IN STANDARD PREPARATION

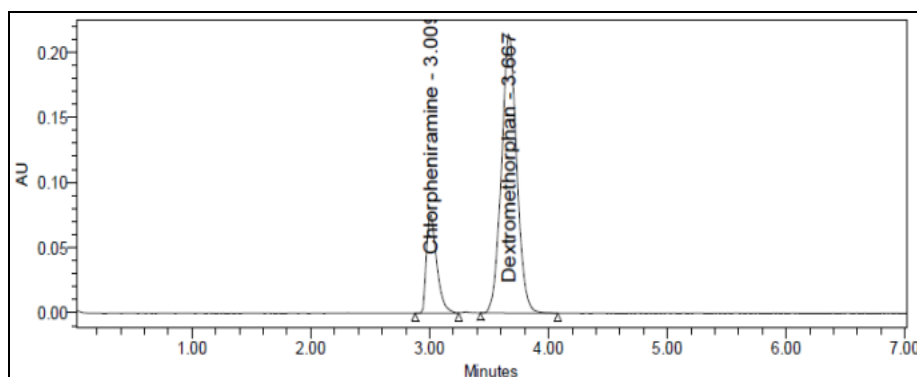


FIG. 2: CHROMATOGRAM OF CHLORPHENIRAMINE MALEATE AND DEXTROMETHORPHAN IN SAMPLE PREPARATION

RESULTS AND DISCUSSION:

Method Validation: The developed RP-HPLC method was validated for parameters like system suitability, linearity, accuracy, precision, LOD, LOQ and robustness according to ICH guidelines¹⁵.

System Suitability: Standard solutions were prepared as per the test method and injected into the chromatographic system. The system suitability parameters like theoretical plates, resolution and asymmetric factor were evaluated. The system suitability parameters were tabulated in **Table 1**. All the parameters were found to be within the limits.

TABLE 1: RESULTS OF SYSTEM SUITABILITY

Analytes	Retention times	Resolution	Theoretical plates	Tailing factor
Chlorpheniramine maleate	3.0 min	-	5751	1.5
Dextromethorphan	3.6 min	4.1	5304	1.0

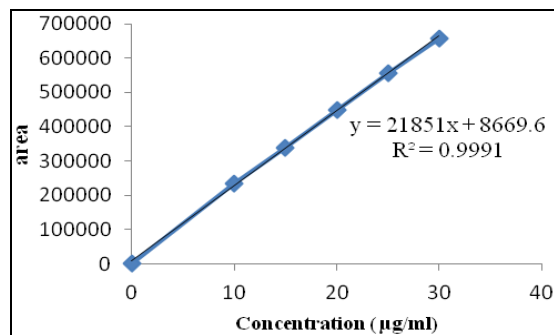
min: minutes

TABLE 2: RESULTS OF METHOD PRECISION

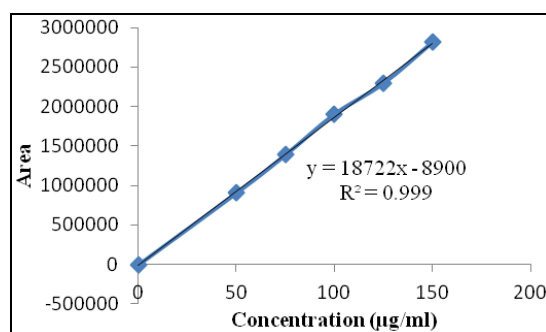
N	Chlorpheniramine maleate		Dextromethorphan	
	Rt (min)	Peak area	Rt (min)	Peak area
Injection 1	3.005	457727	3.665	1920019
Injection 2	3.005	455312	3.666	1931638
Injection 3	3.006	457351	3.665	1927814
Injection 4	3.005	458951	3.674	1919839
Injection 5	3.006	451597	3.670	1910973
Injection 6	3.005	458744	3.666	1925603
Average		456614		1922648
SD		2780.1		7312.3
%RSD		0.6		0.4

Rt: Retention times, # n: number of injections=6

Linearity: The linearity of the test solutions for the assay method was prepared from Chlorpheniramine maleate and Dextromethorphan standard stock solution at five concentration levels from 50% to 150% of assay concentration. The peak area versus concentration data was treated by least-squares linear regression analysis (**Fig. 3 and 4**).

**FIG. 3: LINEARITY CHART OF CHLORPHENIRAMINE MALEATE****Precision:**

Method Precision: The precision of the analytical method was verified by method precision studies. The sample solution was prepared at working concentration and analysis was carried out at replicates. The sample solutions of Chlorpheniramine maleate and Dextromethorphan were prepared as per the test method and injected 6 times into the column. The results of precision were tabulated in **Table 2**. The average was taken; % RSD was calculated and reported. % RSD values were found within the limits, indicating the developed method was precise.

**FIG. 4: LINEARITY CHART OF DEXTROMETHORPHAN**

The results tabulated in **Table 3** have shown an excellent correlation between peak areas and concentration within the concentration range of 10 - 30 µg/ml for Chlorpheniramine maleate, 50 - 100 µg/ml for Dextromethorphan. The correlation coefficients were found to be 0.999 for both the drugs, which meet the method validation

acceptance criteria and hence the method was said to be linear for both the drugs.

Accuracy: To ensure the reliability and accuracy of the method recovery studies were carried out by standard addition method. A known quantity of pure drug was added to pre-analyzed sample and contents were reanalyzed by the proposed method and the percent recovery was reported. The results were given in **Table 4**.

Limit of Detection and Limit of Quantitation: The limit of detection (LOD) and limit of quantitation (LOQ) were established at signal-to-noise ratio of 3:1 and 10:1 respectively. The LOD and LOQ of Chlorpheniramine maleate and Dextromethorphan were experimentally determined by injecting six injections of each drug. The LOD of Chlorpheniramine maleate and Dextromethorphan

was found to be 0.04 µg/ml and 0.11 µg/ml respectively. The LOQ of Chlorpheniramine maleate and Dextromethorphan was found to be 0.14 µg/ml and 0.43 µg/ml respectively.

Robustness: Robustness of the method was verified by altering the chromatographic conditions like mobile phase composition, wavelength detection, flow rate, *etc.* and the % RSD should be reported. Small changes in the operational conditions were allowed and the extent to which the method was robust was determined. A deviation of ± 2 °C in the column temperature and ± 0.2 ml/min in the flow rate, were tried individually. A solution of 100 % test concentration with the specified changes in the operational conditions was injected to the instrument in triplicate. % RSD was reported in the **Table 5**.

TABLE 3: RESULTS OF LINEARITY

Analytes	Correlation coefficient (r^2)
Chlorpheniramine maleate	0.999
Dextromethorphan	0.999

TABLE 4: RESULTS OF ACCURACY

Analytes	Pre-analysed sample conc. (µg/ml)	Amount added (µg/ml)	Amount found (µg/ml)	Recovery (%)
Chlorpheniramine maleate	20	10	9.88	98.83
	20	20	19.65	98.28
	20	30	29.89	99.57
Dextromethorphan	100	50	50.16	100.33
	100	100	98.01	98.01
	100	150	149.61	99.74

TABLE 5: RESULTS OF ROBUSTNESS

Analytes	Flow rate (ml)	% RSD	Column temperature (°C)	% RSD
Chlorpheniramine maleate	0.8	1.2	28	1.4
	1.2	1.1	32	1.3
Dextromethorphan	0.8	0.6	28	1.2
	1.2	0.8	32	1.5

CONCLUSION: The proposed RP-HPLC method was found to be simple, accurate, precise, robust, rapid and economical. This method gives good resolution between two compounds with a short analysis time. Hence this method can be used in quality control departments with respect to routine analysis for the assay of the tablets containing Chlorpheniramine maleate and Dextromethorphan.

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CONFLICTS OF INTEREST: The authors declare that there is no conflict of interest

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