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Research Article

Simultaneous Method Development for Pseudoephedrine Hydrochloride and Desloratadine

Neha Jain [1]*, Amol Kakde [1], Mohan Lal Kori [2]

[1] Faculty of Pharmaceutical Sciences, R.K.D.F. University, Bhopal, M.P., India

[2] Krantisurya Tantya Bhil University, Khargone, M.P., India

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*Address for Correspondence:

Dr. Neha Jain, Professor, Faculty of Pharmaceutical Sciences, R.K.D.F. University, Bhopal, M.P.

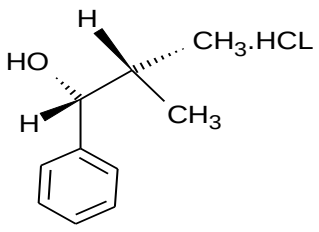
Abstract

Introduction: Chromatographic techniques are primarily used for the qualitative and quantitative analysis of pharmaceutical compounds, drug formulations, and raw materials throughout the drug development process, from the early research phase to the final release of therapeutic products. **Objective:** Simple, accurate, economical and reproducible RP-HPLC method for simultaneous estimation of two component drug mixture pseudoephedrine hydrochloride and desloratadine in combined tablet dosage form. **Material and methods:** Developed HPLC method is reversed phase chromatographic method using inertsil C_{18} column and methanol: ammonium acetate buffer in ratio of 70:30 pH 6.5 adjusted with sodium hydroxide, as mobile phase at a flow rate of 1.0ml/ min. The developed method was validated in terms of specificity, linearity, precision, intermediate precision, accuracy, robustness and solution stability. **Results:** The linearity was observed in concentration range of 12.5-37.5 ug/ml of desloratadine and 450-1350 ug/ml of pseudoephedrine hydrochloride. The results are validated statistically and by recovery studies. The proposed RP-HPLC method achieved satisfactory resolution between desloratadine and pseudoephedrine hydrochloride. It can be used for the synthetic process control and determination of desloratadine in drug substance and pharmaceutical preparation. **Conclusion:** Quality is paramount in all products and services; a 'regulatory analytical technique' is used to evaluate a distinguishing attribute of raw materials, active pharmaceutical ingredients, and pharmaceutical formulations within the pharmaceutical industry. This method is suitable for routine quality control and stability testing of pseudoephedrine hydrochloride and desloratadine in pharmaceutical formulations.

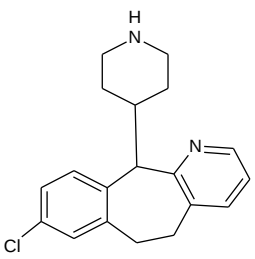
Keywords: RP-HPLC, Simultaneous estimation, Method development, Pseudoephedrine hydrochloride, Desloratadine

INTRODUCTION:

Pseudoephedrine is plant alkaloid with indirect sympathomimetic action. Pseudoephedrine hydrochloride can be used as a bronchodilator in heart block, as mydriatic and as mucosal vasoconstrictor[1]. Alpha adrenergic agonists may be administered topically or orally; they either directly or indirectly interact with the sympathetic nervous system to produce constriction of the microvasculature of the engorged nasal mucosa. Decreased blood flow and venous capacitance results leading to diminished vasculature leakage improved sinus drainage and clearing of the airways[2]. Desloratadine is recently approved for the relief of both nasal and non-nasal symptoms of seasonal allergic rhinitis in adult patients[3,4,5,6]



Pseudoephedrine Hydrochloride



Desloratadine

This work, is a novel, simple, rapid, accurate, precise, selective, rugged, linear and fully validated high-performance liquid chromatography method[1]. A literature search reveals that no method is reported for the determination of pseudoephedrine hydrochloride and desloratadine HPLC[7,8,9,10,11,12,13,14]. The present study aimed to develop and validate HPLC method for the simultaneous estimation of pseudoephedrine hydrochloride and desloratadine. As compared to other analytical techniques, the HPLC method is a highly powerful, quick, automated, accurate, efficient, reproducible, sensitive, and extremely precise analytical technique[15,16,17,]. Solubility studies of pseudoephedrine hydrochloride and desloratadine is evaluated for selection of mobile phase. Since Pseudoephedrine hydrochloride in mobile phase exhibits maximum absorption at 257nm, thus wavelength 254 was chosen for detection Validation of the method for determination of assay will be performed according to the ICH requirements. In the current article, we are reporting the development and validation of a fast, precise, selective, specific, accurate, linear, robustness and rugged high-performance liquid chromatography method

MATERIAL AND METHODS

Chromatographic conditions: A stainless-steel column – C-18, 250 x 4.6 mm, 5 u packed with Octadecylsilane packing (Inertsil). A mixture of 70 volumes of Methanol, 30 volumes of ammonium acetate buffer (3.90 gm/l) and adjusted the pH to 6.5 was used as mobile phase. The mobile phase was filtered through Whatman filter paper No.1 and degassed. Flow rate of 1.0 ml per minute and detection wavelength of 254 nm.

Standard Preparation: Weigh accurately about 180 mg of Pseudoephedrine Hydrochloride and Desloratadine 5 mg working standard to a 100 ml volumetric flask; add 25 ml of mobile phase. Sonicate for 15 minutes. Make up the volume to 100 ml with mobile phase. Further dilute 10 ml of this solution to a 20 ml volumetric flask and dilute up to the mark with mobile phase & mix.

Sample Preparation: Weigh and powder 20 tablets. Weigh and transfer powdered sample equivalent to 180 mg of Pseudoephedrine Hydrochloride and Desloratadine 5 mg to a 100 ml volumetric flask, add 25 ml of methanol. Sonicate for 15 minutes. Make up the volume to 100 ml with methanol. Filter through Whatman filter paper No.1. Further dilute 10 ml of this solution to a 20 ml volumetric flask and dilute up to the mark with mobile phase & mix.

Calibration of HPLC: HPLC calibration was performed by testing the wavelength accuracy, flow accuracy, and compositional accuracy. The system was validated based. HPLC column efficiency was evaluated using a test mixture of benzene and toluene.

System suitability: The standard solution is prepared as given in the procedure and injected in six replicates and the suitability parameters are calculated. The column efficiency, resolution, retention time and asymmetry were calculated for the standard solutions. System suitability parameters may fall within 2% relative standard deviation range during routine performance of the method. The system suitability parameters were calculated. A mixed standards solution containing desloratadine and pseudoephedrine hydrochloride was determined under the proposed conditions, the chromatogram indicating the satisfactory resolution, asymmetry, theoretical plate, retention time.

Specificity: From the graph shows no inference from tablet excipients and mobile phase. No peak was found at retention time of Pseudoephedrine Hydrochloride and Desloratadine. There is no interference from the blank at the retention time of analytes.

Precision:

Repeatability (*method precision):* Six independent samples are prepared and analyzed as per the method. % Assay of Pseudoephedrine Hydrochloride and Desloratadine Tablets in each determination is calculated and the % RSD of the same is determined.

Repeatability of method:

- Weight of the working standard Pseudoephedrine Hydrochloride: 178.6 mg
- Weight of the working standard Desloratadine: 4.9 mg
- Average weight of tablets: 6639 mg.

Repeatability of standard *(System Precision):* Six replicate injections of the standard preparation are made on the system as per the method parameters and the % RSD for peak area and retention time WS determined.

- ***Repeatability of standard (System Precision)***
- Weight of the working standard Pseudoephedrine Hydrochloride: 179.4 mg
- Weight of the working standard Desloratadine: 5.1 mg
- Average weight of tablets: 6646 mg

Intermediate Precision (*Ruggedness):* The intermediate precision was determined by three replicates of the prepared sample solutions. The intermediate precision of the sample application and measurement of peak area was obtained by the assay of three sample sets on different days and instrument. Intermediate precision was carried out by different analyst, day and equipment.

Table 1: Details of variation for equipment

Name of Equipment	***Model***
Balance	Mettler Toledo, AB 204-S
HPLC pump	*Spectra System*
Detector	UV-1100
Auto sampler	Manual Injector
Software	CSW

Accuracy: The accuracy of the methods was assured by the use of the standard addition technique, involving analysis of formulation samples to which certain amounts of authentic drugs were added. The resulting mixtures were assayed, and the results obtained for both drugs were compared to those expected. The recovery experiments were carried out in triplicate by spiking previously analysed sample. Accuracy (recovery in %) evaluated in the range to cover 80% to 120% of stock concentration for Assay of Pseudoephedrine hydrochloride and Desloratadine. Chromatographic conditions are followed as per the method and the criteria for conclusion are analysed.

Linearity: Preparation of Linearity solutions: 5 different solutions of Pseudoephedrine Hydrochloride and Desloratadine ranging from 450 ppm to 1350 ppm and 12.5 ppm to 37.5 ppm respectively and a graph of mean peak area response vs. concentration was plotted.

The linearity of the method was determined five concentrations, the equation for calibration curve was y=1561x+9419.5 (R^2=0.9998) for pseudoephedrine hydrochloride and y=98768x+1119.7 (R^2=0.9999) for desloratadine.

Range: The range of an analytical method was determined by taking the interval between the upper and lower concentration of analyte (including the linearity concentrations)**.**

Range was evaluated % RSD of area, the levels given above data determined the % RSD 0.11 and 0.21 (level 2) of Pseudoephedrine hydrochloride and Desloratadine respectively and the % RSD 0.23 and 0.35 (level 4) of Pseudoephedrine hydrochloride and Desloratadine respectively

Robustness: Standard and sample were prepared as per the method. The sample was analysed against the standard by making variations as per above and the assay calculated for each variation was compared with the assay determined using Precision method. The data is given in below Table 2. Below mentioned changes were designed for confirming the robustness:

Table 2: Changed parameters for robustness

S. N.	Parameter	Changed Value
1	Variation in flow rate	i) -10% Flow Rate and ii) +10% Flow Rate
2	Variation in composition of Mobile phase	-10% Organic phase-methanol +10% Organic phase-methanol
3	Variation in pH	i) -0.2 pH and ii) +0.2 pH

Solution Stability: The stability of the sample solution is checked by injecting this solution stored at room temperature at 0 hour and up to 8 hours. The sample is compared against initially injected standard. The change in the % Assay is calculated for time interval with respect to the initial value.

RESULTS AND DISCUSSION

Specificity: Peak purity analysis is conducted for as such test sample and spiked test sample, which exhibits that there is no interference due to blank. No inference from tablet excipients and mobile phase. No peak was found at retention time of pseudoephedrine hydrochloride and desloratadine. This was very favourable conditions for routine analysis. Pseudoephedrine hydrochloride and Desloratadine peaks are found to be spectrally pure. Hence, proposed method is specific.

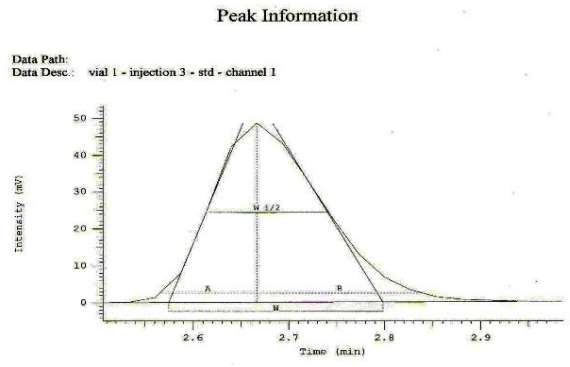


Figure 1: Peak of Pseudoephedrine hydrochloride

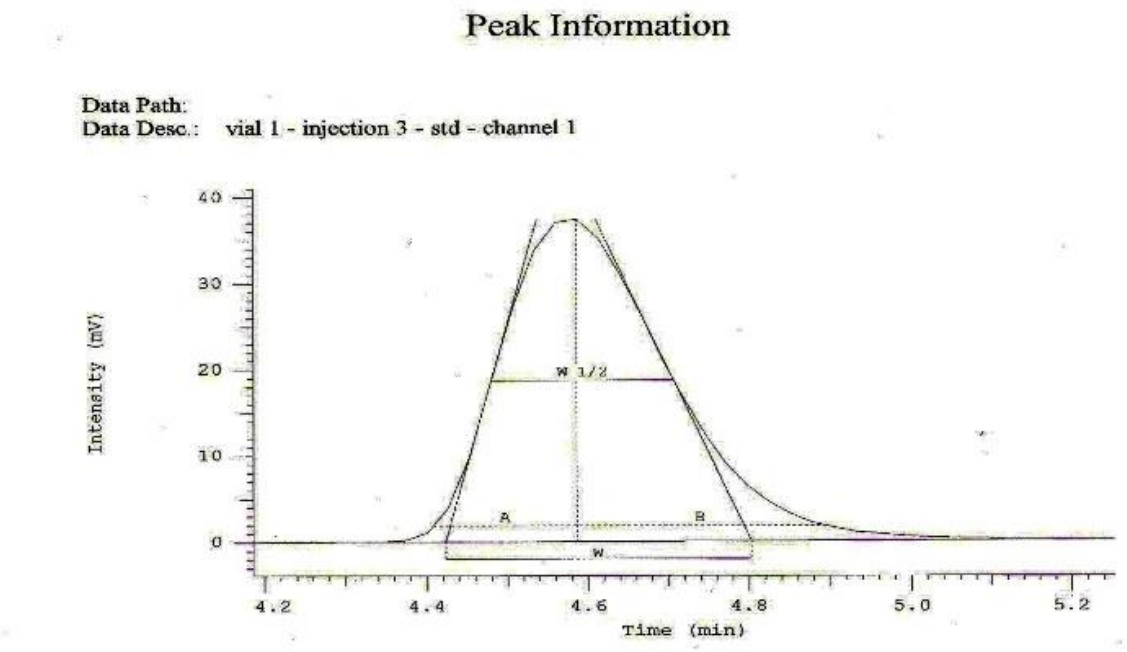


Figure 2: Peak of Desloratadine

The described chromatographic condition achieved satisfactory resolution, reasonable retention and symmetric shape for Pseudoephedrine hydrochloride and Desloratadine, under which the retention times were 2.95 and 4.83 respectively.

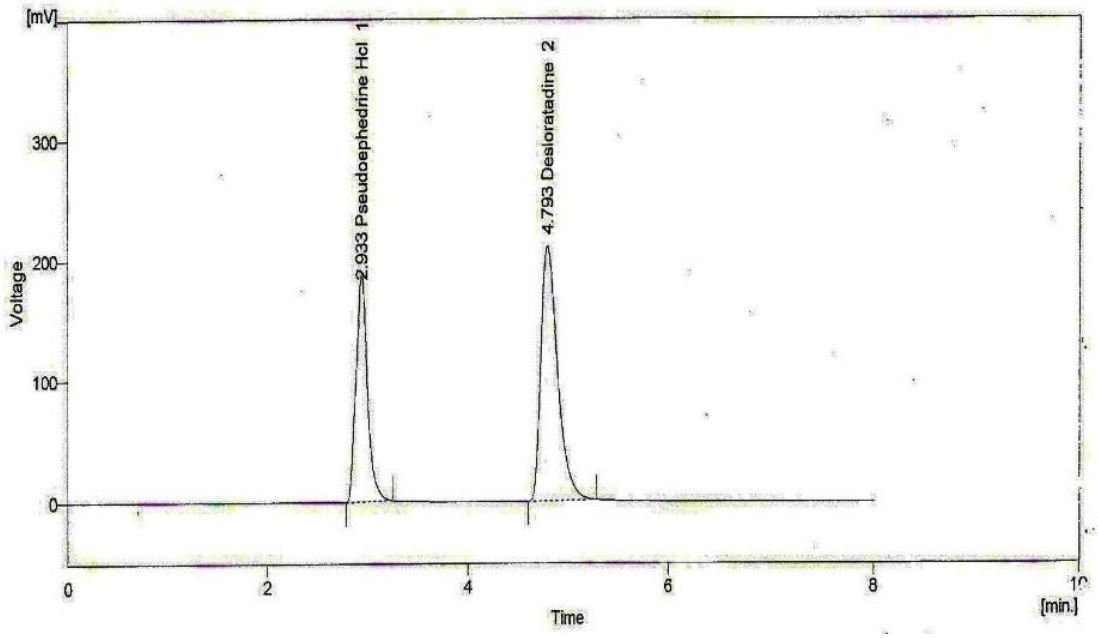


Figure 3: Chromatogram of developed method

Table 3: Results of Specificity

S. No.	Ingredient	Retention time (min)
1	Mobile phase	Not observed
2	Placebo	Not observed
3	Pseudoephedrine Hydrochloride-Std	2.950
4	Desloratadine-Std	4.830
5	Pseudoephedrine Hydrochloride-Sample	3.068
6	Desloratadine- Sample	4.998

Precision and Ruggedness:

System precision: The system precision is evaluated by RSD of peak area of the analyte. The obtained %SD value was 0.52 and 0.81 for pseudoephedrine hydrochloride and desloratadine respectively which is less than 2.0 % meets the acceptance criteria. This indicates good system precision

Method precision: In method precision the % RSD of six individual test results is less than 20.0 %, which meets the acceptance criteria. The obtained %RSD value was 0.45 and 0.35 for pseudoephedrine hydrochloride and desloratadine respectively

Intermediate precision: In the intermediate precision/ruggedness study, six different sample preparations were analysed by different analysts, using different systems, and on different days, the % RS.D. result was found to be less than 2.0 %, and overall % RSD of the test result on comparison with Method precision also found to be less than 2.0 %, thus it is concluded that the method is precise and rugged, meets the acceptance criteria.

Accuracy: The accuracy of the method is checked at 80 %, 100 %, and 120 % of the specification limit. The % recovery for pseudoephedrine hydrochloride and desloratadine obtained is between 80 % to 120 %; meets the acceptance criteria.

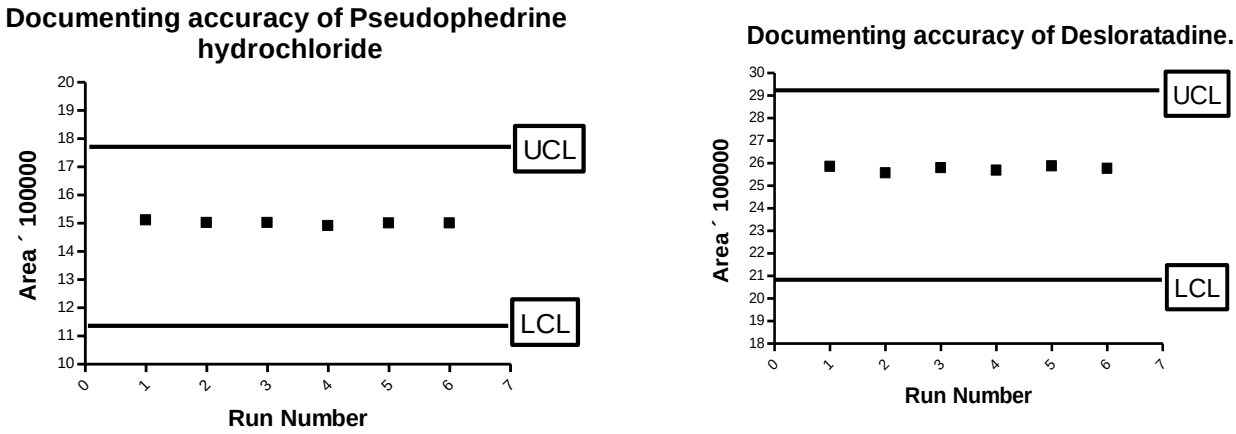


Figure 4: Documenting accuracy graph

Linearity and range: The linearity of the method was determined seven concentrations, the equation for calibration curve was linear. The results show excellent correlation exists between peak area and concentration of drug. The correlation coefficient values are found to be more than 0.98. The proposed analytical method is linear in the range from concentration range of 12.5-37.5 mg/ml for desloratadine and 450-1350 mg/ml for pseudoephedrine hydrochloride. Range was evaluated % RSD of area, the levels given above data determined the % RSD 0.11 and 0.21 (level 2) of Pseudoephedrine hydrochloride and Desloratadine respectively and the % RSD 0.23 and 0.35 (level 4) of Pseudoephedrine hydrochloride and Desloratadine respectively. The results show excellent (% RSD less than 2) range.

Table 4: Data for range of Pseudoephedrine hydrochloride

S. No.	Level 2	Level 2	Level 4	Level 4
	Area	RT	Area	RT
1	1132042	2.808	1688799	2.830
2	1132604	2.800	1695445	2.830
3	1134436	2.792	1695529	2.823
Mean	**1133027**	**2.800**	**1693258**	**2.828**
SD	**1251.8855**	**0.0080**	**3861.5470**	**0.0040**
% RSD	**0.11**	**0.29**	**0.23**	**0.14**

Table 5: Data for range of Desloratadine

S. No.	Level 2	Level 2	Level 4	Level 4
	Area	RT	Area	RT
1	1978863	4.542	2953125	4.565
2	1975002	4.530	2972166	4.570
3	1983447	4.528	2955296	4.558
Mean	**1979104**	**4.533**	**2960196**	**4.564**
SD	**4227.6550**	**0.0076**	**10423.2898**	**0.0060**
% RSD	**0.21**	**0.17**	**0.35**	**0.13**

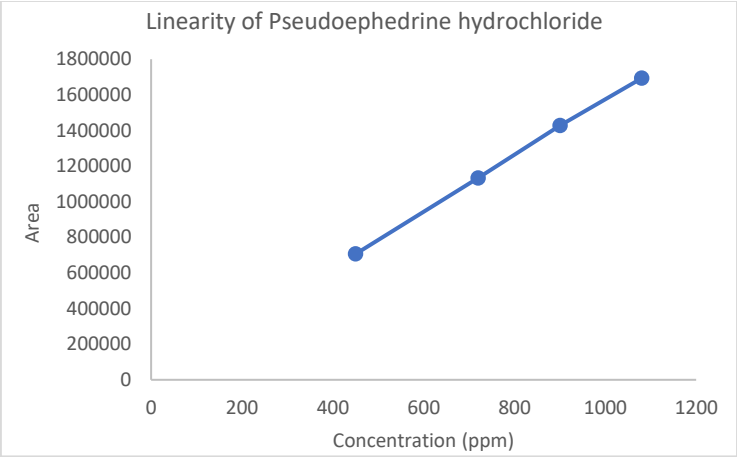


Figure 5: Linearity of Pseudoephedrine hydrochloride

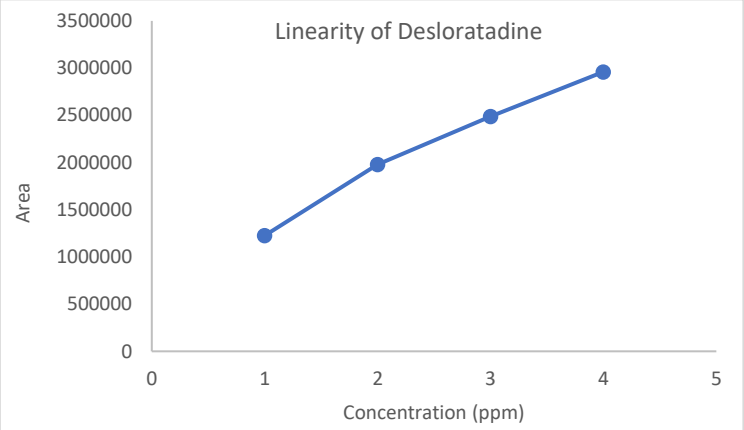


Figure 6: Linearity of Desloratadine

Stability in analytical solution: The results show that for both solutions, the retention time and peak area for both drugs remain almost unchanged (%RSD less than 2) and no significant degradation was observed within the indicated period, indicating that both solutions were stable for at least 8 hr, which was sufficient for the whole analytical process.

Robustness: The validation studies show that the method is robust under deliberately varied conditions of Variation in flow rate of mobile phase (± 10%), Variation in composition of Mobile phase (± 10%) and pH of mobile phase (± 0.2). RRT obtained from each experiment compared with RRT obtained from specificity experiment; meets the acceptance criteria. The robustness, variation in pH of mobile phase composition was evaluated by % RSD, % assay and comparative study with the precision. In the comparison study % RSD and % assay was found to be in acceptable criteria. All the conditions used to evaluate were found to be less than 2(%RSD) so this shows method is robust.

Table 6: Quality control parameters of Pseudoephedrine hydrochloride and Desloratadine

PARAMETER	OBSERVATION			
	Pseudoephedrine hydrochloride		Desloratadine	
Specificity	No interference was found			
Linearity	450 - 1350µg/ml		12.5 – 37.5 µg/ml	
Correlation coefficient (r)	0.99990		0.99998	
Accuracy	**% Recovery**	**RSD**	**% Recovery**	**RSD**
80%	99.5	0.08	100.8	0.20
100%	99.9	0.12	100.8	0.13
120%	100.2	0.05	99.9	0.05
Precision	**% Recovery**	**RSD**	**% Recovery**	**RSD**
Repeatability	99.9	0.45	99.0	0.35
Intermediate precision	101.1	0.13	100.0	0.22
Robustness	**RSD(+)%**		**RSD(-)%**	
	PS	**DL**	**PS**	**DL**
Organic ratio	0.12	0.20	0.43	0.39
pH ratio	0.43	0.87	0.39	0.10
Flow rate	0.82	0.13	0.14	0.61
Solution stability	0.11		0.06	
System suitability	0.35		0.45	

PS- Pseudoephedrine hydrochloride DL- Desloratadine

CONCLUSION:

The developed RP-HPLC method is simple and selective for simultaneous determination of Pseudoephedrine hydrochloride and Desloratadine in combined tablet dosage form was found to be accurate, rapid and economical. The method validation performed by calibrated HPLC with efficient column. The results are validated statistically and by recovery studies. The values of coefficient of variance were satisfactorily low and recovery was close to 100% indicating reproducibility of the method. The linearity was observed within limit hence method is linear.

Developed method for simultaneous estimation of two drugs from combined dosage form is reverse phase chromatographic method utilizing C18 column and isocratic mobile phase, detection of eluent was carried out using UV detector. The method was developed having 8 min. run time only. The excipients in the formulation did not interfere in the accurate estimation of Pseudoephedrine hydrochloride and Desloratadine. The method exhibited high specificity, with clear separation of peaks and no interference from other substances. .

The system precision and ruggedness studies confirmed the method's reproducibility, with relative standard deviation (RSD) values well within acceptable limits. The method precision results had RSDs of less than 10%, confirming its consistency across different conditions, analysts, and instruments. In terms of accuracy, the recovery of Pseudoephedrine hydrochloride and Desloratadine samples ranged between 99.5% and 100.8%, while the method showed excellent linearity (R^2 > 0.99) across a wide concentration range. Finally, the robustness tests demonstrated that the method could withstand variations in experimental conditions without compromising performance. Overall, this validated method is precise, robust, and reliable for the routine analysis and quality control of Pseudoephedrine hydrochloride and Desloratadine. The HPLC method is simple, selective and economical for simultaneous determination of Pseudoephedrine hydrochloride and Desloratadine in the available marketed product "DYL-D" of Ajanta Pharmaceuticals Limited and other pharmaceutical preparations.

Conflicts of Interest: All authors declare that, they have no conflicts of interest in relation to this work.

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Authors Contribution:

Participation in research designing by Dr. Neha Jain, Amol Kakde, Dr. Mohan Lal Kori.

Experiments, Data analysis carryout by Mr. Amol Kakde

Contributors of manuscript writing, editing and drafting are Dr. Neha Jain, Amol Kakde, Dr. Mohan Lal Kori.

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