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Development and Validation of Second Order Derivative Spectrophotometric Method for Simultaneous Estimation of Desloratidine and Pseudoephedrine HCl In Combined Dosage Form

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ABSTRACT

A simple, rapid and specific Second order derivative spectroscopic method with good sensitivity was developed and validated for the simultaneous determination of Desloratidine and Pseudoephedrine HCl in pharmaceutical dosage form. In Ethanol, the quantitative determination of both drugs carried out using second derivatives values measured at 268 and 271 nm for Desloratidine and Pseudoephedrine HCl respectively using a Shimadzu UV-Visible spectrophotometer. In this proposed method both drugs obeyed linearity within the concentration range of 5-30 µg/ml and 80-800 µg/ml for Desloratidine and Pseudoephedrine HCl respectively. The low RSD values indicate good precision and high recovery values indicate accuracy of the proposed method. The proposed method has been applied to the determination of drugs in commercial formulations. Assay results were in good agreement with label claim. The method was validated as per ICH guidelines. The developed method was simple, accurate, precise, specific, sensitive and reproducible which can be efficiently and easily applied to pharmaceutical dosage forms.

Keywords: Desloratidine (DES), Pseudoephedrine HCl (PSE), UV-Visible spectrophotometer, Second Order Derivative Spectroscopy.

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INTRODUCTION

Desloratidine (DES) is chemically 8-chloro-6, 11-dihydro-11-(4-piperdinylidene)-5H benzo [5, 6] cyclohepta [1,2-b] pyridine (Figure 1). Its molecular formula is $C_{19}H_{19}ClN_2$ having molecular weight of 310.82 g/mole. Desloratidine is a tricyclic antihistamine, which has a selective and peripheral H1-antagonist action. It is an antagonist at histamine H1 receptors, and an antagonist at all subtypes of the muscarinic acetylcholine receptor. It has a long-lasting effect and in moderate and low doses, does not cause drowsiness because it does not readily enter the central nervous system.[1] Unlike other antihistamines, desloratadine is also effective in relieving nasal congestion, particularly in patients with allergic rhinitis.[2] Pseudoephedrine(PSE) HCl is chemically (1S, 2S)-2-methylamino-1-phenylpropan-1-ol hydrochloride (Figure 2). Its molecular formula is $C_{10}H_{15}NO$ HCl having molecular weight of 201.7 g/mole. Pseudoephedrine is a diastereomer of ephedrine and is readily reduced into methamphetamine or oxidized into methcathinone. Pseudoephedrine is a sympathomimetic amine. The vasoconstriction that pseudoephedrine produces is believed to be principally a α-adrenergic receptor response.[3] It may be used as a nasal/sinus decongestant, as a stimulant[4] or as an antitussive drug[5] found in many over-the counter preparations, either as a single ingredient or (more commonly) in combination with antihistamines, guaifenesin, dextromethorphan, and/or paracetamol (acetaminophen) or another NSAID (such as aspirin or ibuprofen). Literature survey revealed that there are several methods reported on the determination of DES both in formulation and biological fluids viz: Spectrophotometry[6-7], Spectroflourimetry[8], Densitometry[9], Electrophoresis[10], UPLC[11], and HPLC with detectors like UV[12-14], fluorescence[15], MS[16-21], ESI-MS/MS[22], and GC with nitrogen phosphorus detector[23]. It has been estimated simultaneously in combination with other drugs using RP-UPLC[24], LC-MS[25], and LC-MS/MS[26-27]. Literature survey revealed that PSE has been estimated individually or in combination with other drugs using UV[28-29], Capillary Electrophoresis[30-31], HPLC[32-37] and HPTLC[38].

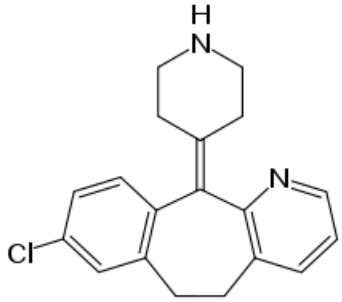

Figure 1: Structure of Desloratidine

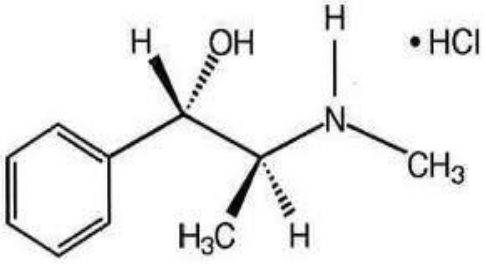

Figure 2: Structure of Pseudoephedrine HCl

Since, No Second order derivative spectrophotometric method has been reported yet for simultaneous estimation of DES and PSE. The present work describes the development of a simple, precise, accurate and reproducible Second order derivative spectrophotometric method for the simultaneous estimation of DES and PSE in Pharmaceutical dosage form. The developed method was validated in accordance with ICH Guideline[39].

MATERIALS AND METHODS

Instruments:

Shimadzu UV-Visible Spectrophotometer (Model UV-1800), Shimadzu digital electronic balance (BL 220H), fast clean ultra sonic cleaning system (Life care equipments Pvt Ltd).

Chemicals:

Analytical pure samples of DES and PSE were provided by Savan Pharmaceuticals and Granules India Pvt Ltd as gift samples respectively. Formulation, Clarinex-D12 (DES-2.5mg + PSE-120mg) manufactured by Shering Corporation was procured from a local pharmacy in Hyderabad. Ethanol is used as solvent.

Methods:

Selection of Solvent:

The derivative spectra's of DES and PSE in different solvents like water and methanol did not show any favorable zero crossing points, but when dissolved in ethanol the derivative spectra's of both drugs showed zero crossing points. Hence ethanol was selected as the solvent for the method.

Selection of derivative method:

Though both first and second derivative spectra's showed zero crossing points in ethanol solvent and their absorbance's were considerably better, but the second derivative method was selected because the spectral characteristics and resolution were good in the second derivative spectra.

Selection of wavelengths (Zero crossing points):

The zero crossing points of Desloratidine were 215, 235, 255, 271 and 286 nm and for Pseudoephedrine were 221, 246, 249, 251 and 268 nm. Out of these wavelengths 271 nm for Desloratidine and 268 nm for Pseudoephedrine were selected as the zero crossing points (Figure 3) for the method based on their linearity data. At 271 nm Desloratidine showed zero absorbance but Pseudoephedrine had considerable absorbance. Similarly at 268 nm Pseudoephedrine showed zero absorbance but Desloratidine had considerable amount of absorbance.

Preparation of DES standard stock solution:

Standard stock solution of DES was prepared by dissolving 10mg of drug in 10ml of ethanol to get a concentration ofµg/ml.

Preparation of PSE standard stock solution:

Standard stock solution of PSE was prepared by dissolving 100mg of drug in 100ml of ethanol to get a concentration of 1000µg/ml.

Validation parameters:

Linearity:

To construct Beer's law plot for DES and PSE different aliquots of DES (0.5- 3ml) with different concentrations (5, 10, 15, 20, 25, and µg/ml) (Figure 4) and PSE (0.8-8.0ml) with different concentrations (80, 160, 240, 320, 400, 480, 560, 640, 720, and µg/ml) (Figure 5) were prepared by serial dilutions with ethanol from individual standard stock solutions. Then Absorbances of these solutions were measured at 268nm (Zero crossing point of PSE) and 271nm (Zero crossing point of DES) for DES and PSE respectively. Linearity values are shown in Table 1.

Precision:

The Precision of the method was established by carrying out the analysis of the analyte using the proposed developed method. The low value of %RSD showed that the methods were precise. The precision values are shown in Table 2.

Limit of Detection (LOD) and Limit of Quantification (LOQ):

The limit of detection (LOD) and limit of quantification (LOQ) of the drugs were derived by calculating the signal-to-noise (i.e. 3.3 for LOD and 10 for LOQ) ratio using the following equations designated by International Conference on Harmonization (ICH) guideline.

$LOD = 3.3 \times \sigma/S$

$LOQ = 10 \times \sigma/S$

Where, σ = the standard deviation of the response S = slope of the calibration curve.

Accuracy (Recovery studies):

The recovery studies were carried out at two different levels i.e. 100% and 50% levels. To assure the reliability of the above method recovery studies were carried out by mixing a known quantity of the standard drug with the reanalyzed sample formulation and the contents were reanalyzed by the proposed method. The % recovery values are shown in Table 3.

Ruggedness:

The ruggedness test of analytical assay method is defined as degree of reproducibility of assay results obtained by the successful applications of assay over different time, day and among

multiple analysts. The % RSD values of assay performed in the same laboratory at two different timings and days shown in the Table 4.

Preparation of Test solutions and Estimation of DES and PSE in Formulation:

For analysis of commercial formulations 5 tablets (Clarinex D12 containing 2.5mg of DES and 120mg of PSE) were weighed, powered and weight equivalent to 5mg of DES and 240mg of PSE was taken and transferred into a volumetric flask and made upto 50ml with ethanol, sonicated for 10min, filtered and further diluted with ethanol to get the required concentration of respective drugs and measured the absorbance at 268 and 271nm for DES and PSE respectively. Then the amount of drugs present in the formulation was calculated and results are shown in Table 4 along with %RSD values.

RESULTS AND DISCUSSION

From the optical characteristics obtained with the proposed method it was found that the drugs obey linearity with in concentration range of 5-30µg/ml for DES and 80-µg/ml for PSE.

From the precision studies it was found that the % RSD is less than 2% which indicates that the method has good reproducibility.

The LOD values of DES and PSE was found to be 0.44µg/ml and 12.48µg/ml respectively and the LOQ values were found to be 1.45µg/ml and 41.21µg/ml respectively.

From the results of recovery studies, it was found that the % recovery values of the pure drugs from the reanalyzed solutions of formulations were in between 99.375-100.5 %, which indicates that the method is accurate and reveals that commonly used excipients and additives present in the pharmaceutical formulations did not interfere in the proposed method.

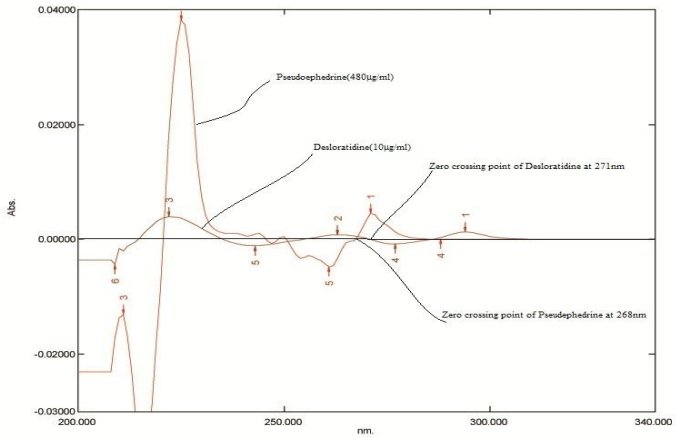

Figure 3: Over lay of Second order derivative spectra's of standard solutions of DES(10µg/ml) and PSE(480µg/ml)

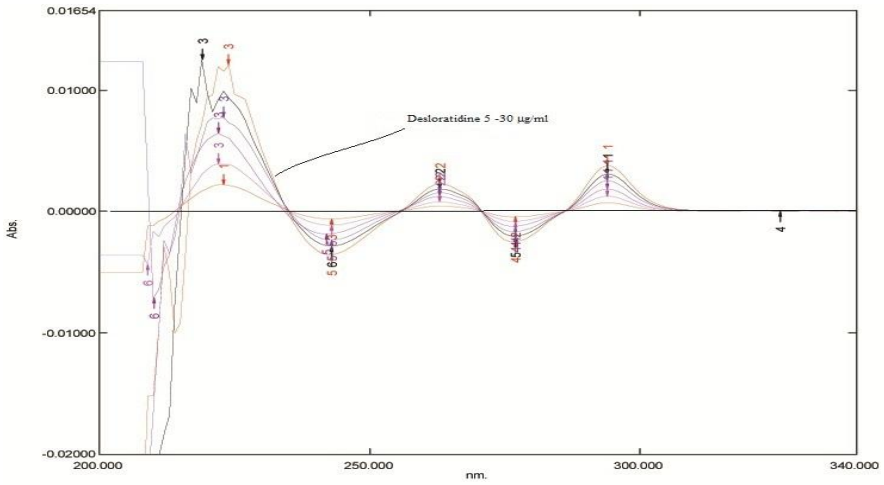

Figure 4: Over lay of second order derivative spectras of DES (5-30µg/ml)

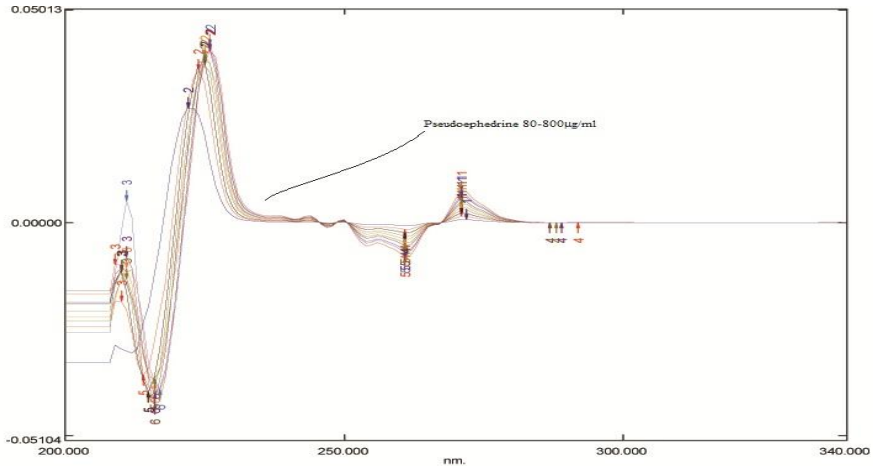

Figure 5: Over lay of second derivative spectras of PSE (80-800µg/ml)

Table 1: Statistical data of calibration curve.

Parameter	DES	PSE
Range	5-30µg/ml	80-800µg/ml
Wavelength(nm)	268	271
Regression equation (y = mx + c)	Y = 0.004x +0.0001	Y = 0.001 +0.001
Slope (m)	0.004	0.001
Intercept (c)	0.0001	0.001
r^2	0.999	0.998

r^2 = correlation coefficient.

Table 2: Precision values of DES and PSE.

Drug	Concentration(µg/ml)	% RSD	
		Intra day	Inter day
DES	5	0.823	1.02
	10	1.31	1.127
PSE	240	1.362	1.117
	480	0.934	1.14

% RSD of three observations.

Table 3: Recovery values of DES and PSE.

Drug	Amount added (µg/ml) (%)	Amount recovered (µg/ml)	% Recovery	% RSD
DES	5 (100%)	5.025,4.985	100.5%,99.7%	0.5651
	2.5 (50%)	2.485,2.495	99.4%,99.8%	0.284
PSE	240 (100%)	238.5,239.3	99.375%,99.71%	0.238
	120 (50%)	119.5,120.3	99.58%,100.25%	0.4742

%RSD of two observations.

Table 4: Analysis of Formulation and its %RSD (Ruggedness Data).

Drug	Label claim (mg)	Amount found (mg)	%Label claim	%RSD
DES	2.5	2.525	101.0%	0.3509
		2.513	100.5%	
PSE	120	121.00	100.83%	0.4361
		120.25	100.21%	

%RSD of two observations (By two different analysts at two different times and days).

The proposed method was simple, sensitive, and reliable with good precision and accuracy. Hence this method can be used for the routine analysis of DES and PSE in bulk and pharmaceutical formulations.

CONCLUSION

A convenient and rapid Second order derivative spectroscopic method has been developed for simultaneous estimation of DES and PSE in available dosage form. The assay provides a linear response across a wide range of concentration. Low intra-day and inter-day %RSD coupled with excellent recoveries. Hence, this method can be easily and conveniently adopted for routine analysis of Desloratidine and Pseudoephedrine in pure form and its dosage forms.

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