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Development of Validated UV Spectrophotometric Stability Indicating Method for Estimation of Desloratadine from Its Tablet Dosage Form

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Abstract
A novel simple, reliable, rapid and accurate UV spectrophotometric stability indicating method (SIM) was developed for estimation of Desloratadine from its tablet dosage form. The study was carried out at 242 nm. Desloratadine has shown linear absorbance over the concentration range of 5-30 µg/mL with R^2 value 0.999. The slope and intercept equation y = 0.045x + 0.013 were used for determination of concentrations of test solution. The proposed method was validated as per ICH Q2 (R1) guidelines for various parameters e.g. precision, accuracy, limit of detection (LOD), limit of quantification (LOQ) and linearity and range. Results of validation study have shown compliance with criteria of ICH guidelines. Relative standard deviation was found less than 2% and recovery was found in range 99.12 – 99.90 %. Method was very sensitive as LOD and LOQ were found to be 0.121 µg/mL and 0.366 µg/mL respectively. Stability indicating potential was studied by analyzing sample subjected to various stress conditions like hydrolysis, oxidation, photo degradation and thermal degradations. Proposed method reveals that Desloratadine was found unstable at hydrolytic and oxidative stress conditions.

Keywords
Stability indicating method, Desloratadine, Validation, ICH guidelines, stress conditions

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INTRODUCTION:

Need for Study:

All pharmaceutical substances un-avoidably contain impurities and the role of ethical pharmaceutical industry is to define an impurity profile that is acceptable for the intended use of a given drug, without compromising its therapeutic safety and efficacy (1-2). The stability of a drug product or a drug substance is a critical parameter which may affect purity, potency and safety. Changes in drug stability can risk patient safety by formation of a toxic degradation product(s) or deliver a lower dose than expected. Therefore, it is essential to know the purity profile and behavior of a drug substance under

various environmental conditions which could be possible by stability testing [3-4].

ICH defined stability indicating assay methods (SIAM) as, quantitative analytical methods that are based on structural, chemical or biological properties of each active ingredient of a drug product and that will distinguish each active ingredient from its degradation products so that the active ingredient content can be accurately measured [5-6].

SIAM can also be defined as "An analytical method that accurately quantitates the active ingredients without interference from the degradation products, process impurities, excipients or other potential impurities" [5].

Validation of a method indicates to establish documented evidence that the system is doing what its purpose to do. Validation is necessary when a method or a procedure is going to be used by a manufacturing company or to be published in any Pharmacopoeias. The validated assay methods will be more accurate, precise and reproducible [7].

Stress testing of the drug can help to identify the degradation products which can help to establish degradation pathways and the intrinsic stability of the molecule and validate stability indicating power for analytical procedures used [8].

Stress testing is performed by exposing drug substances and drug products to extreme conditions, such as pH, photolysis, oxidation and temperature, over a very short time period. It also referred to as forced degradation studies [9-10].

Basic criteria for new method development of SIAM: [11]

The drug or drug combination may not be official in any pharmacopoeias.

A proper stability indicating analytical procedure for the drug may not be available in the literature due to patent regulations.

The existing analytical procedures may require expensive reagents and solvents. It may also involve cumbersome extraction and separation procedures, and these may not be reliable.

Stability indicating assay method provides the support to track the quality of the product from time to time.

Desloratadine [16-19]

8-chloro-6,11-dihydro-11-(4-piperdinylidene)- 5H-benzo[5,6] cyclohepta [1,2-b]pyridine having molecular formula:$C_{19}H_{19}ClN_2$. Desloratadine 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. Unlike other antihistamines, Desloratadine is also effective in relieving nasal congestion, particularly in patients with allergic rhinitis

MATERIAL AND METHOD

Instrument and Material

instrument

Schimadzu 1600 double beam UV/Visible Spectrophotometer

Single pan analytical balance Dhona 200 D

Hot air oven

apparatus

Volumetric flask (10 ml, 50 ml), Beaker, Pipette, Funnel,

Water bath, Burner, Thermometer, Whatmann filter paper #41

chemicals

Drug was obtained from the laboratory.

All chemicals and reagents used were of analytical grade (HCL, NaOH, H_2O_2 and Methanol)

Method

stock solutions: (100 µg/mL)

An accurately weighed 10 mg of pure Desloratadine (DSLR) was transferred to 100 mL volumetric flask and 30 mL methanol was added to it. Solution was shaking for 5 minutes to solubilize compound and final volume was made up to mark with methanol.

working standard solutions:

Appropriate aliquots were withdrawn from the stock solution and diluted up to 10 mL with methanol to obtain standard solutions of different concentrations (5, 10,15,20,25 and 30 µg/mL).

selection of wavelength:

Working standard solution of concentration 10 µg/mL was scanned using spectrophotometer within UV range i,e., 200–400 nm against methanol as a blank. Wavelength 242 nm and 278 nm were selected for absorbance measurement. The UV spectrum of Desloratadine as shown below in Fig.1

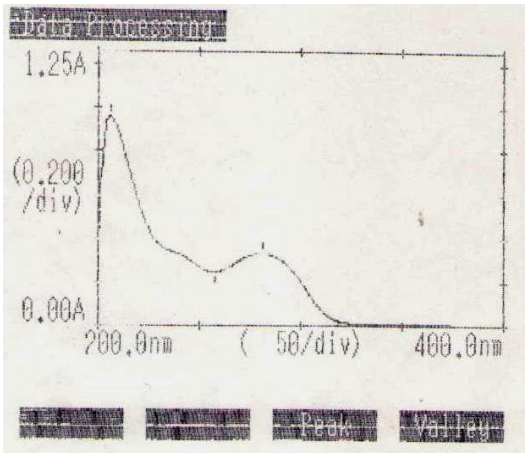


Fig 1. UV Spectrum of Desloratadine

linearity study:
Absorbance of each working solution was measured at the selected wavelength 242 nm. Calibration curve was plotted by taking absorbance on ordinate and concentration on abscissa as shown below in Fig 2.

Table 1. Observations of linearity study

Conc. of DSLR µg/mL	Absorbance at 242 nm
5	0.241
10	0.477
15	0.698
20	0.916
25	1.145
30	1.359

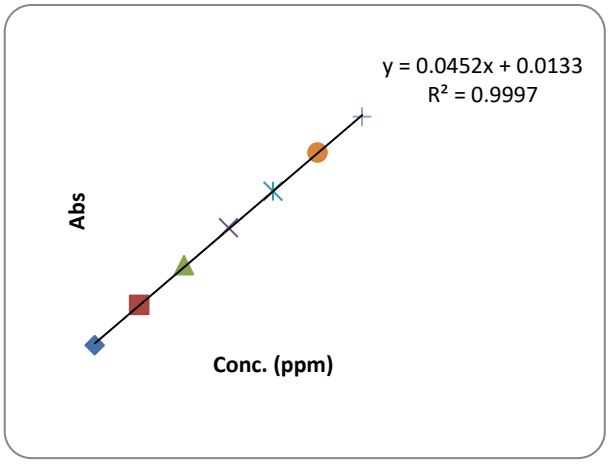


Fig 2. Calibration curve of Desloratadine at 242 nm

Formula:
Concentration of test solutions were calculated by using slope and intercept equation obtained from the calibration curve of Desloratadine.

Slope and intercept equation: **y= m x + c**

Where, y is y axis value i.e. Absorbance of test solution; **x** is x axis value i.e. Concentration of test solution

Slope and intercept equation:

At 242 nm

$$y=0.045\,x+0.013$$

$$x=\frac{y-0.013}{0.045}$$

Assay
An average weight of twenty tablets was determined. Tablets were crushed to fine powder and uniformly mixed. An accurately weighed tablet powder equivalent to 10 mg Desloratadine was transferred to100 ml volumetric flask. Small volume of methanol was added into it and shaked for 5 minutes to dissolve Desloratadine. Excipients were filtered out and filtrate was diluted to 100 ml with methanol. Aliquot about 0.1 ml was taken in 10 ml volumetric flask and volume was made up to the mark with methanol. Procedure was repeated for six times. Absorbance of each solution was recorded at determined at 242 nm and the content of the Desloratadine was found out.

Validation:

Precision: The precision of the proposed method was ascertained by actual determination of three replicates of fixed concentration of the drug within the Beer's range and finding out the percentage purity by the proposed method. Standard deviation and % RSD were calculated for the results [7,17-19].

Aaccuracy

To ascertain the accuracy of the proposed methods, recovery studies were carried out by the standard addition method at three different levels (80%,100 % & 120 %) of concentration of test solution of the tablet [7,12-14].

linearity and range study

Accurately weighed quantity of sample was diluted to obtain concentration in the range of 80-120 % of test concentration. Absorbance of each solution was recorded at 242 nm. It is found that sample obeys linearity over 80 -120 % of test concentration as shown in fig. 3 [7].

rrobustness: Sample was analysed with deliberate modification in method i.e. wavelength for measurement of absorbance has been changed by ± 2 nm as shown in table 46. Three concentrations of sample were studied by measuring absorbance at 240 nm and 244 nm. Results of % content along with SD and % RSD are shown in table 3.

ssensitivity

Sensitivity of the proposed method was determined in terms of limit of detection (LOD) and limit of quantification (LOQ). The LOD and LOQ were calculated using formulae (7,12-14)

$$LOD = 3.3 \times \frac{\sigma}{s}$$

$$LOQ = 10 \times \frac{\sigma}{s}$$

where 'σ' is the standard deviation (n=5) taken as a measure of noise,

and 's' is the slope of the corresponding calibration curve.

Table 2. Result of Assay of Desloratadine

Sr. No.	Wt. of sample in mg	Abs. of std. at 242 nm	Abs. of sample at 242 nm	Conc. (µg/ml)	% DSLR Content
1.	148	0.4642	0.462	9.951	99.57
2.			0.465	10.017	100.21
3.			0.463	9.973	99.78
4			0.465	10.017	100.21
5			0.468	10.084	100.86
6			0.461	9.929	99.35
				Mean	**99.99**
Statistical values for n=6				**SD**	**0.544**
				%RSD	**0.544**

Table 3. Summarized result of validation study

Sr. no	Validation Parameter	Mean	S. D	RSD
1	**Precision**	**99.93**	0.284	0.284
2	**Accuracy**			
2.1	**80 %**	99.57	0.308	0.309
2.2	**100 %**	99.43	0.161	0.162
2.3	**120 %**	99.51	0.385	0.386
3	**Robustness**			
3.1	**240 nm**	99.77	0.541	0.542
3.2	**242 nm**	99. 83	0.430	0.432
3.3	**244 nm**	99.85	0.634	0.635

Table 4. Observation table of Linearity and Range Study

Sr. No.	%Label Claim	Absorbance at 242 nm
1.	80%	0.378
2.	90%	0.418
3.	100%	0.459
4.	110%	0.509
5.	120%	0.554

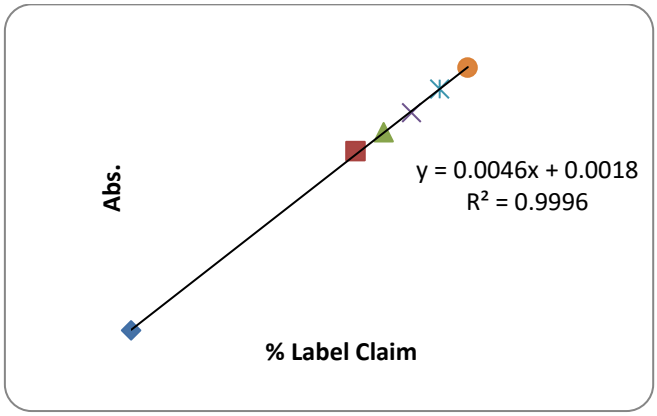


Fig 3. Linear curve of tablet dosage form

Table 5. Result of LOD and LOQ

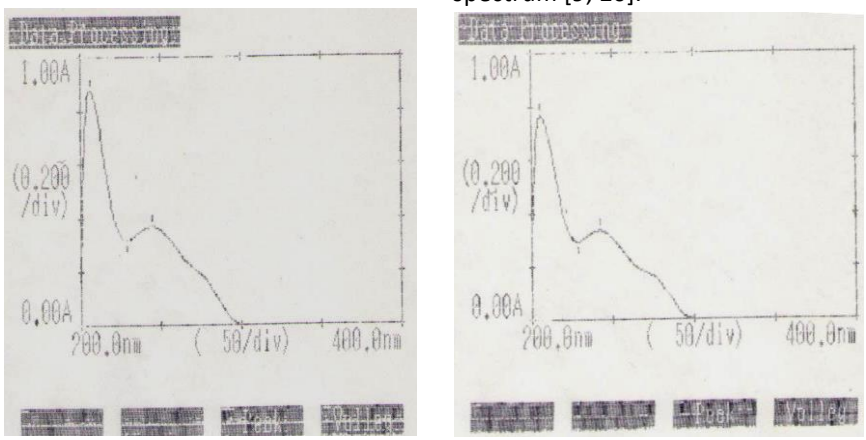
SD (σ)	Slope (s)	$\frac{\sigma}{s}$	LOD (µg/mL)	LOQ (µg/mL)
0.00165	0.045	0.0366	0.121	0.366

Forced Degradation Study

Pure Desloratadine was subjected to various stress condition. UV spectrum of each stressed sample was recorded and compared with standard to check stability of the compound. Absorbance of the sample subjected to acidic, alkaline, thermal and photolytic stress conditions was measured at 242 nm to determine the % degradation. Sample exposed to oxidative stress condition was studied at 278 nm.

Acid Degradation:

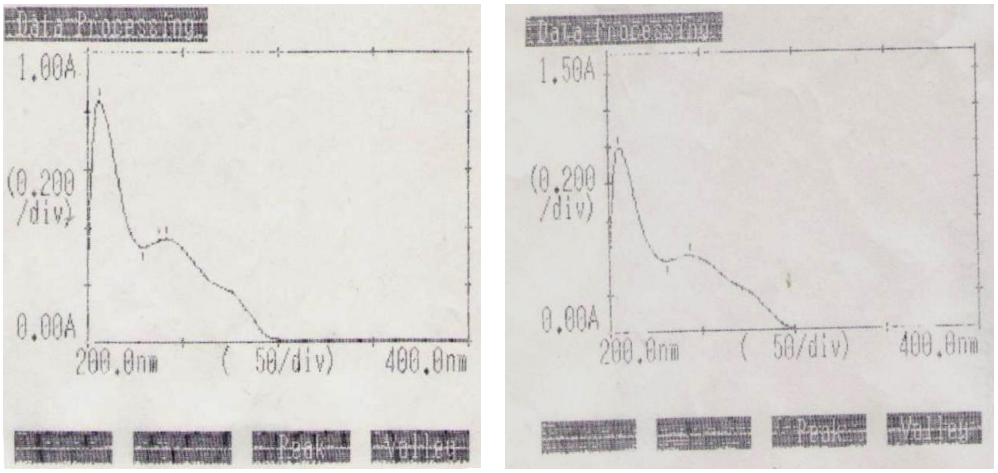
An accurately weighed 10 mg DSLR was taken in two 10 ml volumetric flask and dissolved in 1N and 3 N HCL. Final volume was made up to 10 ml with respective acids. These solutions were refluxed for 8 hours at 80 °C. Aliquots about 0.1 ml were withdrawn from each flask, neutralized and diluted to 10 ml with methanol. UV spectrum was recorded for each solution and compared with standard spectrum [9, 20].



A. B.

Fig 4. Acid degradation sample spectrum of 1N & 3 N HCL at 8 hr as A and B respectively

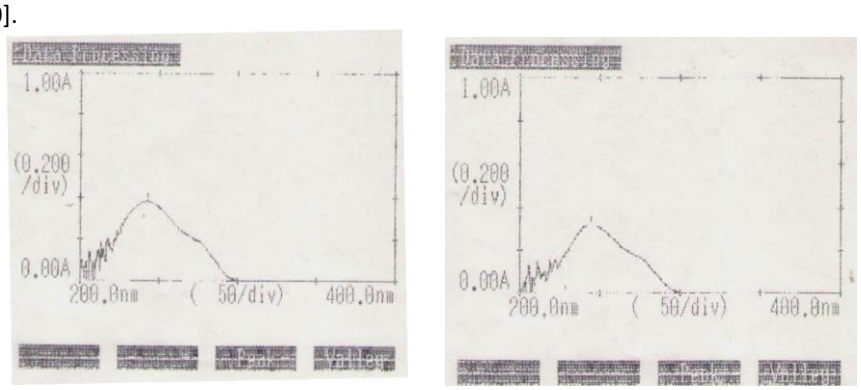
Alkali Degradation: Accurately weighed 10 mg compound was taken in two 10 ml volumetric flask and dissolved in 1N and 3 N NaOH. Final volume was made up to 10 ml with respective alkali. These solutions were refluxed for 8 hours at 80^0c. Aliquots about 0.1 ml were withdrawn from each flask, neutralized and diluted to 10 ml with methanol. Diluted solutions were scanned under 200-400 nm to record UV spectrum and compared with UV spectrum of pure Desloratadine (9, 20).



A. B.

Fig 5. Alkali degradation sample spectrum of 1N & 3N NaOH at 8 hr as A and B respectively

Oxidative Degradation: Accurately weighed 10 mg DSLR was taken in two 10 ml volumetric flask. Approximately 5 ml of methanol was added in each to dissolve the drug. Then 0.3 % v/v and 3% v/v H_2O_2 was added separately to make volume up to the mark. Thereafter solutions were kept for refluxing for 8 hours at 80 °C in water bath. 100 µl portions from each solution were withdrawn and further diluted to 10 ml with methanol. The resulting solution was scanned in the range of 200 - 400 nm against blank prepared by the same way [9,20].



A. B.

Fig 6. 0.3 % v/v and 3%v/v H_2O_2 degraded samples spectrum at 8 hr as A and B respectively

Thermal Degradation: A specific amount of compound was taken in a cleaned Petri dish and placed in an oven at 110 ^{0}C for 12 hours. Then, accurately weighed 10 mg sample was transferred to 10 ml volumetric flask and volume adjusted with methanol. Aliquots about 0.1 ml were withdrawn from stock and diluted to 10 ml with methanol. Diluted solution was scanned under 200-400 nm to obtain UV spectra which further compared spectrum of pure compound [11, 20].

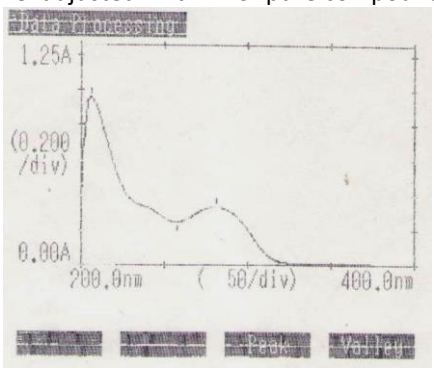


Fig 7. UV Spectrum of Thermal degradation sample

Photo Degradation: A specific amount of compound was taken in a cleaned Petri dish and exposed to radiations of wavelength 254 nm in UV chamber for 12 hrs. Then, 10 mg sample was taken in 10 ml volumetric flask and volume adjusted with methanol. Aliquots about 0.1 ml were withdrawn from stock and diluted to 10 ml with methanol. Diluted solutions were scanned under 200-400 nm to obtain UV spectra which further compared spectrum of pure Desloratadine [20, 21].

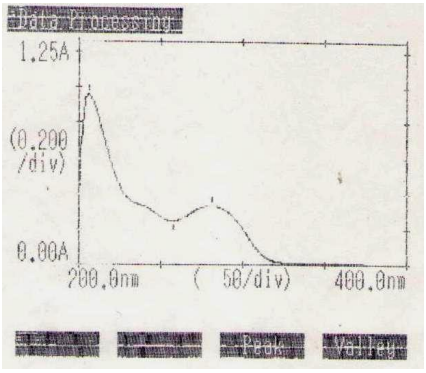


Fig 8. UV spectrum of photolytic degradation sample

Table 6: Summarized Results of forced degradation study

Sr. no	Stress Conditions	Strength	Temp. ^{0}C	Time Hrs	Abs (n=3) 242 nm	Conc. of DSLR µg/mL	Degradation % w/w
1	Acidic	1 N HCL	80	8	0.409	8.75	12.5
2	degradation	3 N HCL	80	8	0.385	8.3	17
3	Alkaline	1 N NaOH	80	8	0.426	8.98	10.2
4	degradation	3 N NaOH	80	8	0.415	8.68	13.2
5	Oxidative degradation	0.3 % H_2O_2	80	8	0.217*	5.32	46.8
6		3 % H_2O_2	80	8	0.210*	5.15	48.5
7	Thermal degradation	----	110	12	0.463	99.67	No degradation
8	Photolytic degradation	ʎ= 254 nm	RT	12	0.465	99.56	No degradation

***Absorbance measured at 278 nm**

RESULT AND DISCUSSION

A simple, sensitive and appreciable stability indicating UV spectrophotometric method has been developed for estimation of Desloratadine from its tablet dosage form. The absorption maxima 242 nm was selected for the study. Absorbance of standard solutions in the concentration range of 5-30 µg/ml was found linear with r^2 value 0.999. The result is expressed in table 2.

The method was fast and economical, and it was also selective and sensitive for the desirable range. Proposed method was validated as per ICH guidelines for precision, accuracy, linearity robustness and sensitivity. Results of study of the aforesaid validation parameters were found satisfactory as statistical values being in range. The method was found precise and reproducible with % RSD value 0.284 as shown in table 3. The accuracy of method was assured by standard addition method and estimating percentage recovery. The method was found accurate and remain unaffected from interfering substances. The results are shown in table 3. Sensitivity of method was determined from linearity equation y = 0.045x +0.013**.** LOD and LOQ were found to be 0.121 µg/mL and 0.366 µg/mL respectively.

Stability indicating capability of proposed method was assured by forced degradation study. The study was carried out by subjecting Desloratadine to various stress conditions e.g. Acidic and basic pH, oxidative, thermal and photo degradations. UV spectra of acidic, alkaline and oxidative stressed samples were not match with spectrum of pure Desloratadine. Therefore, it could be concluded that Desloratadine underwent acid, alkali and oxidative degradation. However, UV spectra of thermal and photolytic stressed samples found identical to standard spectrum indicating thermal and photo stability of Desloratadine at 110 ^{o}C up to 12 hrs.

Summarized results of forced degradation study shown in table 6.

CONCLUSION:

The proposed analytical method was validated as ICH Q2 guidelines. It was found simple, rapid, precise, accurate, sensitive and linear. The present study has also proven stability indicating potential of method. This proposed UV spectrophotometric SIM can be used in routine analysis of Desloratadine.

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