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UV-Spectrophotometric Estimation of Olopatadine hydrochloride in Bulk and Pharmaceutical Dosage Form by Zero, First and Second Order Derivative Methods

Smita. S. Aher[1]*, Jayshree. S. Gawali[2], Ravindranath B. Saudagar[1]

[1] Department of Pharmaceutical Chemistry, R. G. Sapkal College of Pharmacy, Anjaneri, Nashik 422213, Maharashtra, India

[2] Department of Pharmaceutical Quality Assurance, R. G. Sapkal College of Pharmacy, Anjaneri, Nashik – 422213, Maharashtra, India

ABSTRACT

Simple and accurate UV spectrophotometric methods by Zero, First and Second order derivative method have been developed and validated for the estimation of Olopatadine hydrochloride in bulk and its pharmaceutical dosage form. The standard and sample solutions of Olopatadine hydrochloride were prepared in methanol and water. Olopatadine hydrochloride was estimated at 299, 289 and 267 nm for the derivative UV-spectrophotometric method. Beer's law was obeyed in the concentration range of 20 to 120 µg / mL with coefficient of correlation value 0.9996, 0.999 and 0.999 for Zero, First and Second order derivative method. These methods were tested and validated for various parameters according to ICH and USP guidelines. The precision expressed as relative standard deviation were of less than 2 for the above three methods respectively. The proposed methods were successfully applied for the determination of Olopatadine hydrochloride in pharmaceutical dosage form. Results of the analysis were validated statistically and were found to be satisfactory. The proposed methods are simple, easy to apply, low-cost and require relatively inexpensive instruments.

Keywords: Olopatadine HCl, UV-Visible spectrophotometry, Pharmaceutical Dosage forms, Derivative Spectroscopy, Method validation.

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***Address for Correspondence:**

Jayshree. S. Gawali, Department of Pharmaceutical Chemistry. R. G. Sapkal College of Pharmacy, Anjaneri, Nashik 422213, Maharashtra, India

INTRODUCTION

The chemically Olopatadine hydrochloride is {(11Z)-11-[3-(di-methyl-amino) propylideine]-6, 11-dihydrodibenzo [b, e] oxepin-2-yl} acetic acid, hydrochloride. (Figure1) corresponding to the molecular formula ($C_{21}H_{23}$ NO_3.HCl). Olopatadine HCl has a relative molecular mass of 373.873 g/mole. [1 ,2, 3, 4]

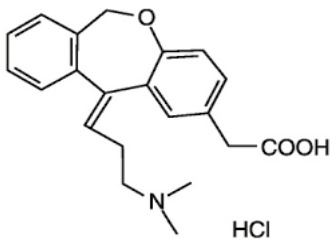

Figure 1. Chemical structure of Olopatadine Hydrochloride

Olopatadine HCl is a selective histamine H1 receptor-antagonist activity and inhibits the release of histamine from mast cell. It is used to treat itching associated with allergic conjunctivitis. Its principal effects are inhibition of H1 receptors. They act on the bronchi, capillaries, and other smooth muscles.[3, 1]

The literature survey reveals that numerous methods for determinations of Olopatadine HCl in single in pharmaceutical dosage forms,[4,5,6] spectrophotometric methods in combination with other drugs [7,8], HPTLC [9,10], stability indicating spectrophotometric [11,12], HPLC methods in combination with other drug including HPLC [13,14] and UPLC method in bulk and pharmaceutical dosage form[15]. In this study we described very simple, sensitive, novel spectrophotometric methods. These methods show very simple, precise, cost effective and accurate approach for the analysis of Olopatadine HCl. For these methods there is no need of sophisticated instruments,

expensive solvents or a large number of samples.

MATERIALS AND METHODS

Pure sample of Olopatadine HCl was kindly supplied as a gift sample by Aurobindo Pharmaceuticals (Hyderabad, Maharashtra) India. All solvents and chemicals were of analytical grade. Marketed Tablet dosage form used in this research work was WINOLAP 5mg (SUN PHARMA) acquired from local market.

Instruments

Spectrophotometric measurements were carried out on Shimadzu UV 1800 double beam spectrophotometer. Infrared spectroscopic study was done on FTIR (Bruker, Japan) .

Preparation of standard stock solution

Standard stock solution of Olopatadine Hydrochloride was prepared by accurately weighing 100 mg of Olopatadine Hydrochloride to 100 ml volumetric flask with 10 mL of methanol. The drug was sonicated and volume was made up to mark with water to get the concentration of 1000 µg/ml.

Selection of analytical wavelength for zero order derivative method

0.1mL of the standard stock was pipette out and transfers to 10 ml volumetric flask and volume was made up to mark with water. The solution was than scanned in UV range between 200-400nm UV-VIS Spectrophotometer, Shimadzu, Japan to determine the absorption maxima of the drug against blank as water. The absorption maxima were found to be 299 nm and it is shown in Figure 2.

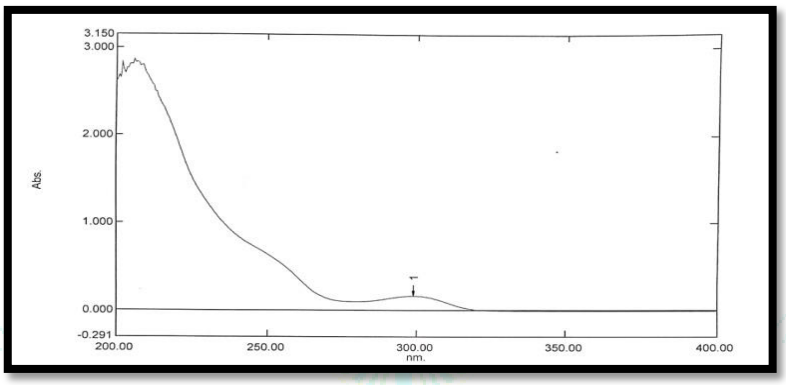

Figure 2. Zero Order Derivative Spectra of Olopatadine HCl

Selection of analytical wavelength for First order derivative method

The 0.1 mL of the standard stock was pipette out and transfers to 10 ml volumetric flask and volume was made up to mark with water. The solution was scanned in the wavelength range of 200 - 400 nm using UV spectrophotometer. The conversion of normal spectrum into first order derivative spectrum was done. The spectrum shows the sharp peak and maximum absorbance at 289 nm. The λ_{max} 289 nm was selected for the first order derivative analysis and it is shown in Figure 3.

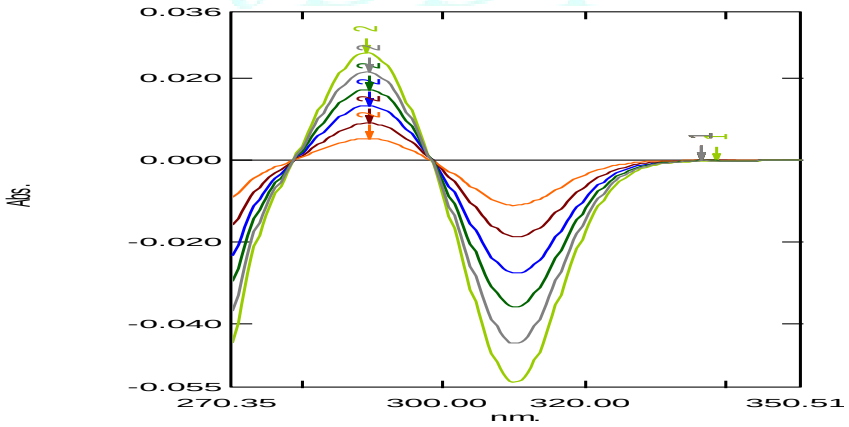

Figure 3. First Order Derivative Spectra of Olopatadine HCl

Selection of analytical wavelength for Second order derivative method

The 0.1 mL of the standard stock was pipette out and transfers to 10 ml volumetric flask and volume was made up to mark with water. The solution was scanned in the wavelength range of 200 - 400 nm using UV spectrophotometer. The conversion of normal spectrum into first order derivative spectrum was done. The spectrum shows the sharp peak and maximum absorbance at 267 nm. The λ_{max} 267 nm was selected for the first order derivative analysis and it is shown in Figure 4.

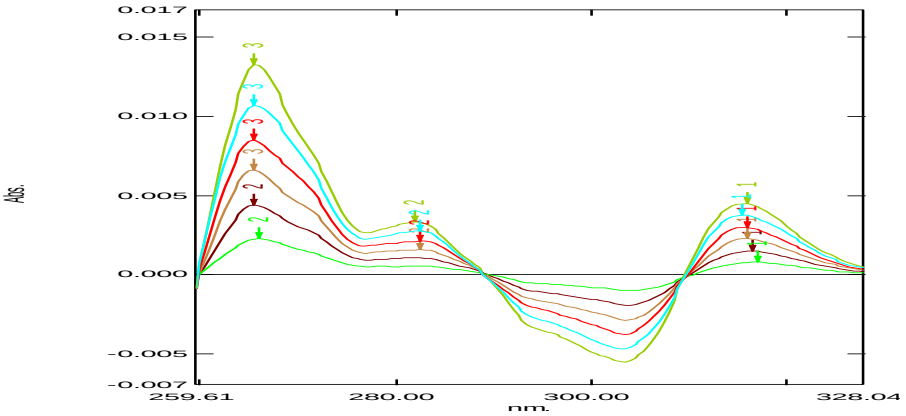

Figure 4. Second Order Derivative Spectra of Olopatadine HCl

Preparation of calibration curve for Zero, First and Second order derivative methods

Aliquots portion 0.2, 0.4, 0.6, 0.8, 1.0, 1.2 mL was pipetted out from the standard stock solution and transferred to series of 10 mL volumetric flask and volume was made with water to get the concentration range from 20-120µg/ml. The absorbance was measured three times for each concentration. Absorbance of each solution was measured against water as blank at 299 nm and 289nm and 267 nm for zero order, first order and Second order methods respectively.

Analysis of tablet formulation

Twenty tablets were weighed and finely powdered. Equivalent to 10 mg of Olopatadine HCl was weighed and transferred to a 100 ml volumetric flask containing with specific 10 mL of methanol and sonicated for 20 minutes. The solution was filtered through 0.45µm Whatmann filter and volume was made up to mark with water and mixed to get 100µg/ml. An aliquot of tablet stock solution 3 ml was transferred to 10 ml volumetric flask and volume was made up to mark with water to get concentration of 10µg/ml of Olopatadine HCl. Recovery study of tablet formulation is shown in Table 1.

Table 1. Result for tablet analysis (Label Claim)

Parameters	Zero Order	First Order	Second Order
Tablet	Winolap (5 mg)	Winolap (5 mg)	Winolap (5 mg)
Mean*(n=6)	101.35	100.28	98.92
SD	0.37	1.06	0.54
% RSD	0.36	0.06	0.55

RESULTS AND DISCUSSION [16,17,18]

Method validation

The method of analysis was validated as per the recommendations of ICH and USP for the parameters like accuracy, linearity, precision, detection limit, quantitation limit, ruggeddness and robustness.

$$SD = \frac{\sqrt{\sum(X - \bar{X})}}{N - 1} \qquad \%\ RSD = \frac{SD}{Mean} \times 100$$

SD: Standard Deviation

%RSD: Relative standard deviation **N:** Number of data values in data set **X:** Each of values of the data set

Linearity

The linearity of proposed derivative methods was evaluated by plotting the absorbance against concentrations of standard drug solutions. Stock solutions was consequently diluted with water to get 20, 40, 60, 80, 100, 120 µg/mL. The λmax for first and second order derivative was obtained by converting the normal spectrum of zero order spectrum to first order spectrum and second order spectrum. The correlation coefficient was found to be 0.9996, 0.999 and 0.999 for zero order, first order and Second order derivative method. The result for calibration curve of zero, first and second order derivative spectrophotometric method shown in Figure 5, 6, 7.

Result for Linearity:

Preparation of calibration curve

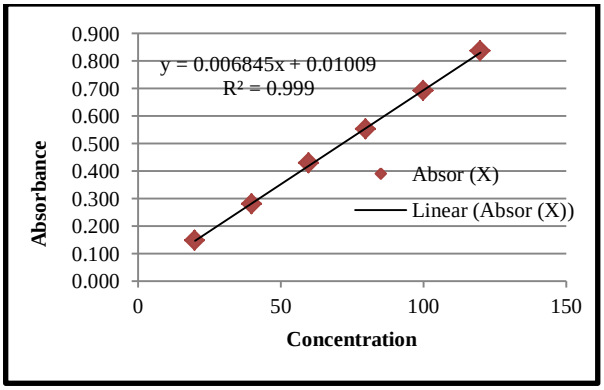

Figure 5: Calibration curve for Olopatadine HCl by Zero Order spectrophotometric method

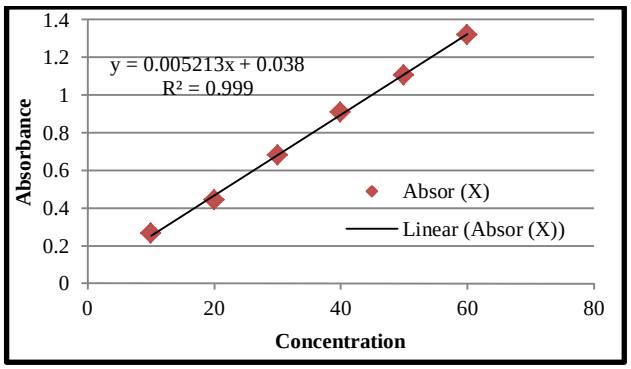

Figure 6 : Calibration curve for Olopatadine HCl by First order spectrophotometric method

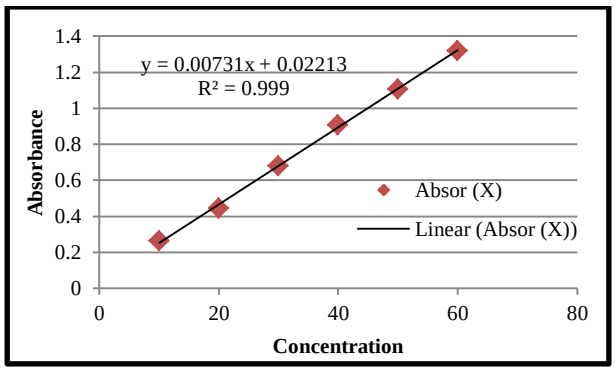

Figure 7: Calibration curve for Olopatadine HCl by Second order derivative spectrophotometric method

Precision

The Precision study of analytical method validation express the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of day precision of proposed methods was evaluated by analysing the three different independent concentrations i.e. 40, 60, 80 µg/ml in triplicate. These concentrations were evaluated for three consecutive days and the results are given in Table 2, 3 and 4 for zero order, first order and second order derivative spectrophotometric method.

Table 2: Result for Precision Study for Intra-Day and Inter- Day (Zero Order).

	Conc.	Intra-Day Precision		Inter-Day Precision	
Statistical Analysis	**(µg/ml)**	**Amount Found (n=3)**	**%RSD**	**Amount Found (n=3)**	**%RSD**
Statistically the terms like SD and %RSD calculated in presented study. The standard values are mentioned In ± SD	40	99.83±0.70	0.71	99.02±0.93	0.94
	60	101.25±0.74	0.73	100.64±0.61	0.60
	80	101.34±0.24	0.23	101.02±0.52	0.51

Table 3 :Result for Precision Study for Intra-Day and Inter-Day (First Order)

Conc	Intra-Day Precision		Inter-Day Precision	
(µg/ml)	**Amount Found (n=3)**	**%RSD**	**Amount Found (n=3)**	**%RSD**
40	101.99±0.0006	0.23	100.87±0.0020	0.81
60	102.09±0.0034	0.95	100.92±0.0034	0.94
80	101.11±0.0037	0.81	100.87±0.0015	0.33

Table 4: Result for Precision Study for Intra-Day and Inter-Day (Second Order)

Conc	Intra-Day Precision		Inter-Day Precision	
(µg/ml)	**Amount Found (n=3)**	**%RSD**	**Amount Found (n=3)**	**%RSD**
40	101.64±0.0006	0.18	100.95±0.0025	0.79
60	99.53±0.0005	0.13	100.36±0.0015	0.33
80	99.04±0.0061	1.01	99.72±0.0041	0.69

Accuracy

The accuracy of an analytical procedure expresses the results obtained by that method to the true value. The accuracy of the developed method was determined on the basis of recovery studies. The recovery tests were performed by adding known quantity of pure standard drug into the solution of tablet powder. The sample was then spiked with standard at levels 50%,100% and 150% of tests concentrations. The resulting spiked sample solutions were analysed in triplicate. The result for accuracy shown in Table 5.

Table 5: Result for accuracy (Recovery) Study

Zero Order		First Order		Second Order	
Level of addition	**% recovery (n=3)**	**Level of addition**	**% recovery (n=3)**	**Level of addition**	**% recovery (n=3)**
50%	99.81±0.0026	50%	100.180	50%	100.82±0.0026
100%	99.08±0.0011	100%	99.993	100%	99.33±0.0011
150%	99.82±0.0012	150%	99.049	150%	101.17±0.0015

Limit of Detection (LOD) Limit of Quantitation (LOQ)

The LOD and LOQ were evaluated from the data obtained from calibration curve. The LOD and LOQ for zero order derivative method was found to be 0.530µg/ml and 1.607µg/ml respectively, for first order derivative was found to be 0.863µg/ml and 2.877µg/ml and for second order derivative method was found to be 0.616µg/ml and 2.052µg/ml respectively.

Robustness

Robustness of an analytical procedure is the measure of its capacity to remain unaffected by small but deliberate variations in method parameters. The robustness study of proposed method was evaluated by changing parameters like wavelength. In the proposed method the robustness study was studied by changing the wavelength (297 and 301) for zero order and (287 and 291) for first order derivative methods and (265 and 269) for Second Order derivative. The robustness testing for both the methods are given in Table 6, which indicates that, no significant difference was observed in results. Thus, it's demonstrated that the methods are robust.

Table 6. Result for Robustness Study

Parameters	Zero Order		First Order		Second Order	
	Wavelength 297 nm	**Wavelength 301 nm**	**Wavelength 287 nm**	**Wavelength 291 nm**	**Wavelength 265 nm**	**Wavelength 269 nm**
Conc.(µg/mL)	**40 µg/mL**	**40 µg/mL**	**30 µg/mL**	**30 µg/mL**	**60 µg/mL**	**60 µg/mL**
Mean (n=5)	0.280	0.277	0.158	0.186	0.532	0.614
±SD	0.0016	0.0016	0.0016	0.0023	0.0049	0.0039
% RSD	0.5725	0.5787	1.012	1.2259	0.9265	0.6406

Ruggedness

Ruggedness is the degree of reproducibility of the results obtained under a variety of conditions. Ruggedness study was performed to examine effect of non-procedure related factors such as instruments and analyst. Ruggedness study of Olopatadine HCl was carried out by using two different analyst under the similar operational and environmental conditions. The % RSD for zero order, first order and second order derivative for change in analyst was found in limit (< 2%) which is shown in Table 7.

Table 7. Result for Ruggedness Study

Parameters	Zero Order		First Order		Second Order	
	Analyst I	**Analyst II**	**Analyst I**	**Analyst II**	**Analyst I**	**Analyst II**
Conc. (µg/mL)	**30 (µg/mL)**	**30 (µg/mL)**	**20 (µg/mL)**	**20 (µg/mL)**	**80 (µg/mL)**	**80 (µg/mL)**
Mean(n=5)	0.213	0.275	0.121	0.119	0.531	0.576
±SD	0.000752	0.00233	0.0008	0.0016	0.006	0.004
% RSD	0.3537	0.8491	0.6213	1.344	1.089	0.742

Specificity

Specificity study is the ability to asses unequivocally the analyte in the presence of component which may be expected to be present. For the specificity study of proposed method the sample may be spiked with excipients or possible interfering components. Results of specificity study were found in analytical limits shown in Table 8.

Table 8. Result for Specificity Study

Level of Addition	Std. drug conc.	Exipients Conc.	Total conc.	Zero Order		First Order		Second Order	
	(µg/mL)	**(µg/mL)**	**(µg/mL)**	**Abs.**	**% RSD**	**Abs.**	**%RSD**	**Abs.**	**%RSD**
50%	20	40	60	0.150	0.38	0.145	0.39	0.177	0.33
100%	40	40	80	0.279	0.35	0.247	0.40	0.312	0.67
150%	60	40	100	0.429	0.23	0.351	0.59	0.461	0.13

In proposed method % RSD was found to be less than 2%. The method is highly sensitive and entirely suitable for routine analysis of Olopatadine HCl in bulk and solid dosage forms.

CONCLUSION

The developed analytical method for Olopatadine HCl by zero order derivative, first order derivative and second order derivative spectroscopic methods was found to be linear, specific, rapid and precise. The solvent used in proposed methods is methanolic water is an economical and cheap, which indicates that the proposed methods are economic and cost effective. The %RSD for all validation parameters studied.

Conflicts of Interest:

None.

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