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METHOD DEVELOPMENT AND ITS VALIDATION FOR SIMULTANEOUS ESTIMATION OF MONTELUKAST SODIUM AND OLOPATADINE HYDROCHLORIDE AS API AND IN TABLET DOSAGE FORM BY UV SPECTROSCOPY

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Abstract: A new, rapid, precise, selective and sensitive UV spectroscopy method is developed for the simultaneous estimation of montelukast sodium and olopatadine hydrochloride in combined dosage form. In the developed method, absorbance was measured at 283 nm (λ_{max} of montelukast sodium) and 299 nm (λ_{max} of olopatadine hydrochloride). The drugs obeyed the Beer's law in the concentration range of 2-14 µg/ml and 1-7 µg/ml respectively for montelukast sodium and olopatadine hydrochloride. Accuracy of the method was determined by recovery studies and was found to be 100.01 % and 100.25 % for montelukast sodium and olopatadine hydrochloride respectively. The developed method is simple, precise, rapid and selective. It can be used for routine analysis of both drugs in bulk as well as in pharmaceutical formulations.

Keywords: Simultaneous Equation Method, Montelukast sodium, Olopatadine hydrochloride, Validation.

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INTRODUCTION

Montelukast sodium[1] is chemically 1-[[[(1R)-1-[3-(1E)-2-(7-chloro-2-quinolinyl) ethenyl]phenyl]-3-[2-(1-hydroxy-1.-methylethyl)phenyl]propyl]thio]-methyl]-cyclopropaneacetic acid, monosodium salt. Selectively antagonist leukotriene D_4(LTD_4), at the cysteinyl leukotriene receptor, cys LT_1,in the human airway montelukast inhibit action of LTD_4 at the $cyst_1$ receptor, preventing airway edema, smooth muscle contraction and enhance secretion of thick viscous mucous.

Olopatadine hydrochloride[2] is chemically 2-[(2Z)-2-[3-(dimethylamino)propylidene]-9-oxatricyclo[9.4.0.0{3,8}]pentadeca-1(11),3(8),4,6,12,14-hexaen-5-yl]acetic acid. It is a selective histamine H_1 antagonist that binds to the histamine H_1 receptor. This blocks the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine. Olopatadine is devoid of effects on alpha-adrenergic, dopamine and muscarnic type 1 and 2 receptors[3-4].

A literature survey[5-12] regarding quantitative analysis of these drugs revealed that there were several analytical methods for montelukast sodium using extractive spectrophotometry, HPLC and HPTLC, RP-HPLC. Extractive spectrophotometry, RP-HPLC, HPTLC methods have been reported for estimation of olopatadine hydrochloride. There is only first order derivative spectroscopic method is reported for the estimation of montelukast sodium. So in present study simple, sensitive, specific, accurate and precise spectroscopic method is described for the estimation of these two drugs in combined dosage forms.

MATERIAL AND METHOD:

MATERIAL

Apparatus: Instrument used was an UV-Visible double beam spectrophotometer, shimadzu (model UV-1800) with a pair of 1 cm matched quartz cells.

Reagents and Chemicals: Montelukast sodium was kindly supplied as a gift sample from Cipla Ltd. Solan (India). Olopatadine hydrochloride was kindly supplied as a gift samples from Sun Pharma Ltd, Sikkim (India).

METHOD

Preparation of Standard Solution:[13-15] The standard stock solution of Montelukast sodium and Olopatadine hydrochloride was prepared by dissolving 10 mg of each API in 10 ml of different volumetric flask with distilled water to produce 10 mg/ml of each solution.1ml of aliquot was

taken in 10ml volumetric flask and diluted with distilled water to prepare standard stock solution of 100 µg/ml of each.

Selection of analytical wavelength:[16-17] Standard solutions of Montelukast sodium(10 µg/ml) and Olopatadine hydrochloride(5 µg/ml) were scanned in the range of 200 to 400 nm for the determination of wavelength having maximum absorbance. Montelukast sodium shows 283 nm Olopatadine hydrochloride shows 299 nm and as the wavelength having maximum absorbance. From the overlain spectra, For the simultaneous equation method, 283 nm and 299 nm were selected as analytical wavelengths.

Method development:

For the selection of analytical wavelength for the simultaneous estimation[18], the stock solutions of montelukast sodium and olopatadine hydrochloride were separately diluted with methanol, to obtain the concentrations of 10µg/ml montelukast sodium and 5µg/ml scanned in the wavelength range of 200-400 nm. The λmax of montelukast sodium and olopatadine hydrochloride were found to be 283 nm (λ1) and 299 nm (λ2) respectively. For the construction of calibration curve, standard solutions of montelukast sodium and olopatadine hydrochloride were diluted in the range of 2-14 µg/ml and 1-7 µg/ml respectively.

In Simultaneous equation method[19], the absorbance of the solution was measured at 283 nm and 299 nm and concentration of the two drug was calculated using

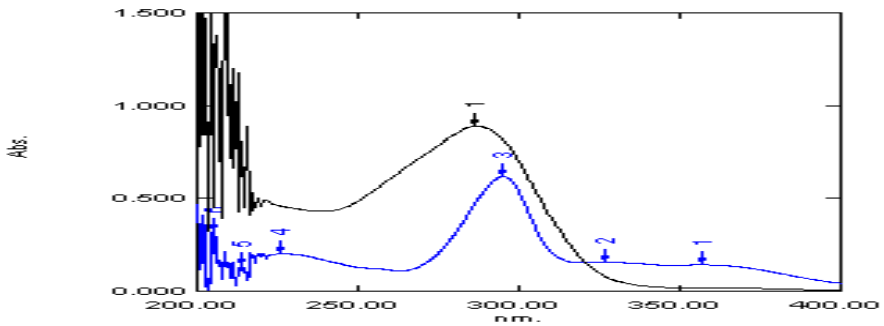
$$Cx=A2\ ay1- A1\ ay2 / ax2\ ay1- ax1\ ay2 \quad \text{(Eqn.1)}$$

$$Cy=A1\ ax2 -A2\ ax1 / ax2\ ay1- ax1\ ay2 \quad \text{(Eqn.2)}$$

Where, Cx and Cy are concentration in g/100 ml of montelukast sodium and olopatadine hydrochloride respectively.

ax1 is the absorptivity of montelukast sodium at 283 nm, ax2 is the absorptivity of olopatadine hydrochloride at 299 nm,

ay1 is the absorptivity of montelukast sodium at 299 nm, ay2 is the absorptivity of olopatadine hydrochloride at 283 nm.



Overlain Spectra of Montelukast sodium and Olopatadine hydrochloride

Table 1: Optical Parameter and Regression Characterstic of Montelukast sodium and Olopatadine hydrochloride

Parameters	Montelukast sodium		Olopatidine hydrochloride	
	283 nm	299 nm	283 nm	299 nm
Beers's law limit (μg/ml)	2 – 14	2 – 14	1 – 7	1 – 7
Molar absorptivity (l mole^{-1}cm^{-1})	3.72 x 10^3	2.95 x 10^3	7.14 x 10^3	6.32 x 10^3
Sandell's sensitivity (mg/cm^2/.001absorbance unit)	0.047	0.039	0.052	0.013
Régression équation (y= a + bc)				
slope (b)	0.062	0.066	0.105	0.116
intercept (a)	0.030	0.027	0.024	0.058
Correlation coefficient (r^2)	0.999	0.999	0.998	0.998

VALIDATION OF ANALYTICAL METHOD

The developed method was validated statistically as per ICH guidelines Q2(R1)[20] for all the parameters.

Like accuracy, linearity, precision and specificity. Accuracy of the method was established on the basis of recovery studies, carried out by standard addition method in which pre-analyzed samples were taken and standard drug was added at three different levels (80%, 100% and 120% of the test concentration). Result of recovery studies and percentage recovery were found to be satisfactory and are reported in (**Table 2).** The linearity of the method was established from the spectra by measurement of absorbance of standard solutions containing varying concentrations of each compound. Linearity was found for montelukast sodium 2-14 μg/ml (r2 < 999) and olopatadine hydrochloride 1-7 μg/ml (r2 < 998). Precision of the method was demonstrated by intraday and interday variation studies. In intraday variation study three replicates of solutions at three concentration level 6.4, 8, 9.6 μg/ml for montelukast sodium and 3.2, 4, 4.8 μg/ml for olopatadine hydrochloride were carried out. Similarly intraday precision was also carried out by repeating analysis for three days and concentrations were calculated results were ascertained by % RSD < 2. Specificity of the method was ascertained by analyzing standard drug in presence of excepients, which shows no interference at all. **(Table 3)**

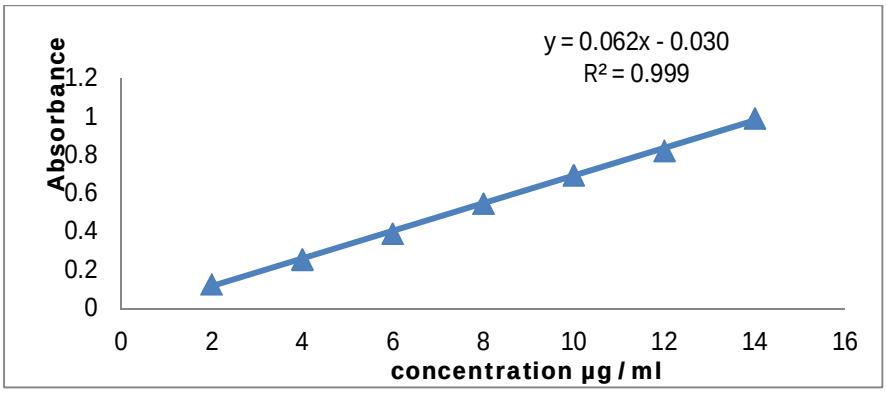
Assay of Tablet Dosage Form:

The quantity of API weighed about and used in preparation mentioned as 11.4 mg (~10) Montelukast and 5.3 mg (~5) of Olopatadine. Actual quantity weighed accurately was used to calculate quantity of powder equivalent to 10 mg of Montelukast sodium and 5 mg of Olopatadine hydrochloride. The triturated drug mixture was transferred to 100 ml volumetric flask and mixed with 70 ml of methanol as a solvent. Solution was sonicated for 20 minutes there after volume was made up to 100 ml with same solvent. The solution was filtered through Whatmann filter paper 42. From the filtrate, 8 ml was transferred to 100 ml volumetric flasks and volume was made up to the mark with methanol as a solvent to produce the resultant solution of 80 μg/ml and 40 μg/ml of Montelukast and Olopatadine respectively. Further from the above solution, 1 ml was transferred to five different 10 ml volumetric flasks and volume in each was made up to mark with methanol as a solvent. Absorbance of these solutions was measured at 283.0 nm and 299.0 nm using methanol as blank. . The concentrations of two drugs in sample were determined by using equations 1 and 2[21-23]. The results are reported in the (**Table 4)**.

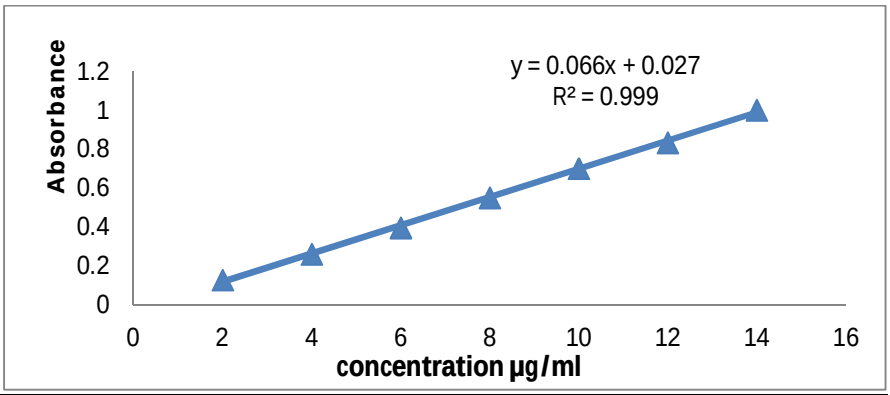
RESULT AND DISCUSSION

The proposed method was validated as per ICH guideline Q2(R1). Method discussed in the present work provides a convenient and accurate way for simultaneous analysis of montelukast sodium and olopatadine hydrochloride. In UV spectroscopy method, wavelengths selected were 283 nm and 299 nm (λ_{max}) The plot of absorbance versus respective concentrations of montelukast sodium and olopatadine hydrochloride were found to be linear in the

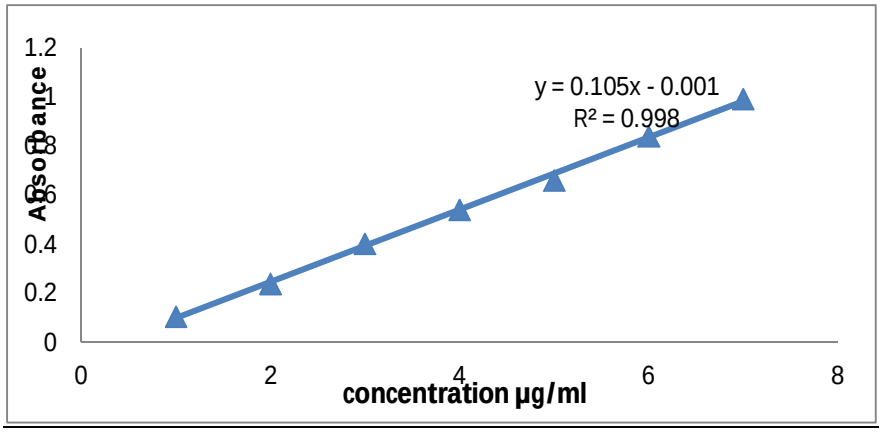
concentration range of 2-14 µg/ml for montelukast sodium and 1-7 µg/ml for olopatadine hydrochloride with correlation coefficient 0.999 at 283 nm and 0.998 at 299 nm as shown in table 3 and figures 2-4. Precision was calculated in terms of repeatability, intraday and interday variations and % RSD was found to be in acceptance range (table 3). The accuracy of method was determined by standard addition method. The % recovery ranges from 100-01% for montelukast sodium and 100.25% for olopatadine hydrochloride (table 1).



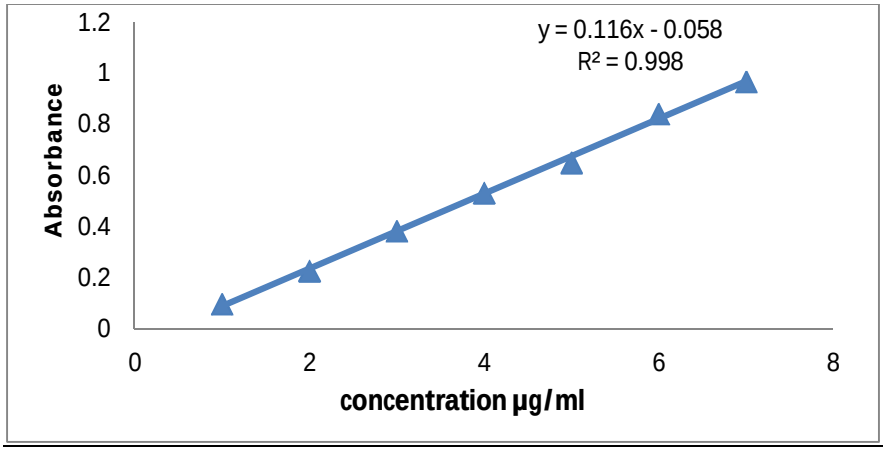
Calibration curve of Montelukast sodium at 283



Calibration curve of Montelukast sodium at 299



Calibration curve of Olopatadine hydrochloride at 299



Calibration curve of Olopatadine hydrochloride at 283

Table 2: Recovery Study

Mixture	Wavelength (nm)	Mean Recovery ± SD	% RSD
MONTE:OPOL	283 nm	Montelukast sodium	Montelukast sodium
		100.01 % ± 0.016	0.02
	299 nm	Olopatadine hydrochloride	Olopatadine hydrochloride
		100.25 ± 0.296	0.30

Table 3: Validation Parameter

Validation parameters		MONTE	OLOP
Specificity		% interference <0.5 %	
Range (µg/ml)	Working range	0.831-14	0.190-7
	Linearity range	2-14	1-7
	Target range	6.4, 8, 9.6	3.2, 4, 4.8
	Target concentration	8	4
Precision (%RSD)	Repeatability	0.77	0.50
	Intra day	0.763	0.470
	Inter day	0.752	0.556
Accuracy (% recovery)		100.01	100.25
LOD (µg/ml)		0.274	0.063
LOQ (µg/ml)		0.831	0.190

Table 4: Estimation of Montelukast sodium and Olopatadine hydrochloride in tablets by UV Spectroscopy

Label claim (mg)	Conc. Mean in µg/ml	%Mean ± SD	% RSD
10 mg MONTE + 5 mg OLOP	MONTE 9.959 ± 0.156	MONTE 99.662± 0.204	0.022
	OLOP 4.926 ± 0.149	OLOP 99.14± 0.214	0.301

CONCLUSION

The low value of relative standard deviation for repeated measurement indicates that the method is precise. The value of % recovery is approximately 100%, which indicates that the method can be used for estimation of these two drugs in combined dosage forms without any interference due to the other components present in the formulations. Hence this study presents simple, accurate, precise and rapid spectroscopic analytical method for the simultaneous estimation of these two drugs in combined dosage form.

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