International Journal of Pharmaceutical Research and Development (IJPRD)
Platform for Pharmaceutical Researches & Ideas
www.ijprd.com

DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR SIMULTANEOUS ESTIMATION OF MONTELUKAST SODIUM AND OLOPATADINE HYDROCHLORIDE IN BULK AND FORMULATED DOSAGE FORM.

Sucheta B Rananavare[1]*, Dr.Vijay R Salunkhe[1]

[1]Rajarambapu College of Pharmacy, Kasegaon-415404,Maharashtra, India.

ABSTRACT

A simple, rapid, accurate, precise, and economic Spectrophotometric method for simultaneous estimation of montelukast sodium and olopatadine hydrochloride in bulk and formulated tablet dosage form has been developed. Method is based on solving simultaneous equation. Montelukast sodium and olopatadine hydrochloride shows absorbance maximum at 345 and 206 nm respectively, so absorbance was measured at the same wave lengths for the estimation of montelukast sodium and olopatadine hydrochloride. Both drugs obey the beer lamberts' law in the concentration range of 2-20µg/ml and 1-10µg/ml for montelukast sodium and olopatadine hydrochloride respectively. Method is validated according to ICH guideline and carried out for analysis of montelukast sodium and olopatadine hydrochloride in pure and formulated tablet dosage form.

KEYWORDS : *Montelukast sodium, Olopatadine hydrochloride, New approved dosage form, UV-Spectrophotometer, Simultaneous equation, Validation.*

Correspondence to Author

Sucheta B Rananavare

Rajarambapu College of Pharmacy, Kasegaon-415404,Maharashtra, India.

Email: suchetarananavare@gmail.com

INTRODUCTION

Montelukast sodium (MONT) is [R-(E)]-1-[[[1-[3-[2-(7-chloro-2quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl] thio] methyl] cyclopropane acetic acid, monosodium salt. Montelukast is a specific cysteinyl leukotriene receptor antagonist belonging to styryl quinolines [1].The cysteinyl leukotrienes (LTC4, LTD4, LTE4) are potent inflammatory eicosanoids which is found in human airway (including airway smooth muscle cells and airway macrophages) and on other Pro-inflammatory cells (including eosinophils and certain myeloid stem cells) and it is released from various cells including mast cells and eosinophils. In allergic rhinitis, CysLTs are released from the nasal mucosa after allergen exposure during both Early- and late-phase reactions and are associated with symptoms of allergic rhinitis. Intranasal challenge with CysLTs has been shown to increase nasal airway resistance and symptoms of nasal obstruction. Montelukast is an orally active compound that binds with high affinity and

Selectivity to the CysLT1 receptor. Montelukast inhibits physiologic actions of LTD4 at the CysLT1 receptor without any agonist activity.[2]

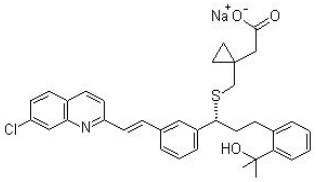

Figure No.-1 Structure of montelukast sodium

Olopatadine hydrochoride has the chemical name {(11Z)-11-[3-(dimethylamino) propylidene]-6, 11-dihydrodibenzo [b,e] oxepin-2-yl} acetic acid. It is a white, crystalline powder.Olopatadine is an antihistamine and mast cell stabilizer. It is a selective inhibitor for the release of histamine and other pro-inflammatory mediators from the mast cell.[3] Olopatadine hydrochloride is a potent, selective histamine H1 antagonist that inhibits the in vivo and in vitro type 1 immediate hypersensitivity reaction including inhibition of histamine induced effects on human conjunctival epithelial cell.[4]They act on bronchi, capillaries and other smooth muscles. Olopatadine is inhibitor of the release of the histamine from mast cells.[5]The structure of olopatadine hydrochloride. (Figure No.-2)

MATERIALS AND METHODS

Instruments

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu) with a pair of matched quartz cell of 1cm width was used for measuring absorbance. Elder digital balance was used for weighing and ultra sonicator of prama instruments used for sonicating the drug and sample solution.

Materials

Montelukast sodium was kindly gifted from Melody pharma, Mumbai and olopatadine hydrochloride from Indoco remedies, Mumbai. The formulated tablets (Lable clam: montelukast sodium 10 mg and olopatadine hydrochloride 5 mg) used for analysis. All chemicals used for development were analytical grade.

Selection of solvent wavelengths

Drugs should have adequate absorbance in the same solvent for the simultaneous determination. The structure of montelukast sodium (Figure No.-1)

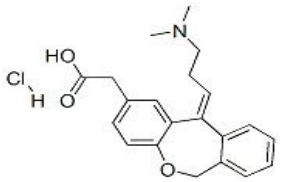

Figure No.-2 Structure of Olopatadine hydrochloride

In distilled water, montelukast sodium was not totally dissolved, possibility of water as solvent was ruled-out. In methanol, olopatadine hydrochloride absorbs at 206 nm and montelukast sodium absorbs at 345 nm, hence methanol was selected as a possible solvent for analysis. These two wavelengths were selected for development of simultaneous equation.

Preparation of standard stock solution

About 10mg of montelukast sodium and olopatadine hydrochloride pure drug was weighed accurately and transferred into 10ml volumetric flask. The volume was made up to 10ml using methanol to obtain a solution that has a concentration 1000 µg/ml. 1ml of this stock solution was taken and then diluted up to 10 ml using methanol to obtain a solution that has a concentration 100 µg/ml which is standard stock solution.

Preparation of sample stock solution

Randomly selected formulated and optimized tablets were weighed initially and crushed to powder. Powder quantity equivalent to 10 mg each of montelukast sodium and 5mg olopatadine hydrochloride was weighed. The powder was dissolved in a sufficient volume of methanol and filtered through a Whatman filter paper of 125mm. Filtrate was made up to 10 mL with methanol, 1 mL of filtrate was transferred to 10 mL volumetric flasks, and then the volume was made up with methanol. Absorbance of this solution at 345 nm and 206 nm was recorded.

Procedure for calibration curve

To a series of 10ml volumetric flasks, carefully transferred aliquots of standard drug solution of montelukast Sodium and olopatadine hydrochloride (0.2 to 2 ml and 0.1 to 1

ml)respectively and the volume was made with the diluents. Calibration curve was recorded by taking absorbances on ordinates and concentration of the standard Montelukast Sodium and olopatadine hydrochloride.

VALIDATION OF THE DEVELOPED METHOD[6, 7]

Linearity

For each drug, appropriate dilutions of standard stock solutions were assayed as per the developed methods. For method the Beer- Lambert's concentration range was found to be 2-20µg/mL for montelukast sodium and 1-10µg/mL for olopatadine hydrochloride.

Accuracy

The recovery study was carried out as 80%, 100% and 120% of the test concentration as per ICH Guidelines. The recovery study was performed three times at each level.

Precision: Interday and Intraday precision

The interday and intraday precision was determined by assay of the sample solution on the intraday precision was determined by assay of the sample solution on the same day and on different days at different time interval respectively.(six replicate)

Ruggedness study

This study is carried out within laboratories and variation like different analyst. Ruggedness of the methods was assessed by carrying out assay 3 times with different analyst by using same equipment.

Limit of Detection

The detection limit is determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be reliably detected.

$$LOD = 3.3 (SD / S)$$

Where SD = the standard deviation of the response
S = the slope of the calibration curve

Limit of Quantitation

The quantitation limit is generally determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be quantified with acceptable accuracy and precise.

$$LOQ = 10 (SD / S)$$

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

RESULT

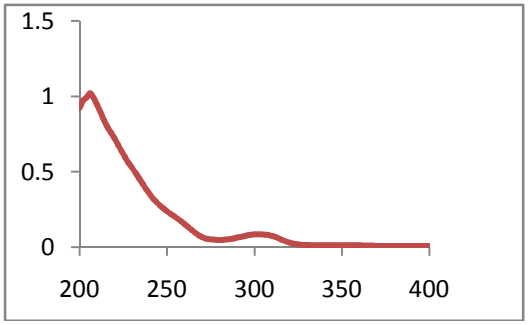

Figure No.-3: Spectra of olopatadine hydrochloride

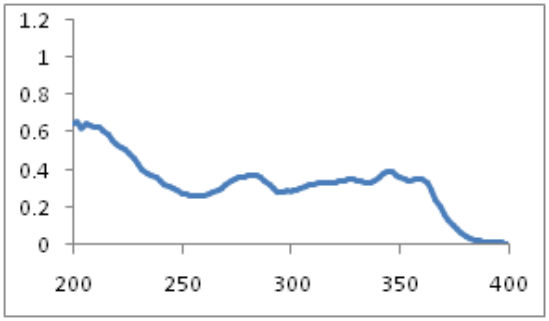

Figure No.-4: Spectra of montelukast sodium.

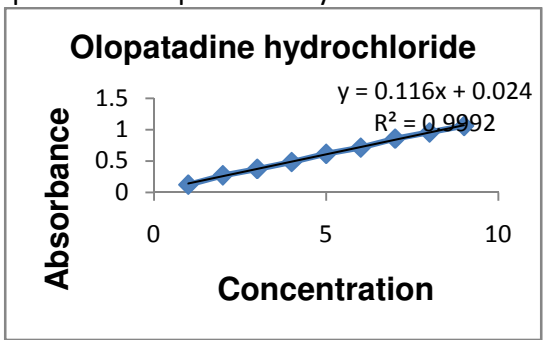

Figure No.-5: Calibration curve of olopatadine hydrochloride.

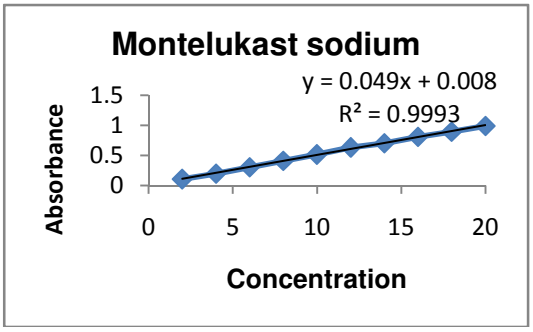

Figure No.-6: Calibration curve of montelukast sodium.

Parameter	Olopatadine HCL	Montelukast sodium
Wavelenth detection	206	345
Slop	0.1186	0.049542
Intercept	0.01677	0.01033
Correlation coefficient	0.9993	0.9992
Range	1-10µg /mL	4-28µg /mL
Regression equation	Y=0.116x+0.024	Y=0.049x+0.008
Limit of detection	0.07 µg /mL	0.208µg /mL
Limit of quantitation	0.2 µg /mL	0.63 µg /mL

Table 1: Result of Validation parameters.

Drug	Interday precision		Intraday precision	
	%Amount Found ± SD*	% RSD	%Amount Found ± SD*	% RSD
Olopatadine hydrochloride	100.08 ± 0.2617	0.2619	99.85 ± 0.2449	0.2445
Montelukast sodium	99.77 ± 0.4457	0.4446	99.76 ± 0.2928	0.2920

*Average of six determinations **Table No.2:-**Result of precision

Percentage level		% RSD		% RSD
	%Recovery ± SD*		%Recovery ± SD*	
80%	101.4 ± 0.755	1.343	97.66 ± 1.310	1.26
100%	99.6 ± 0.5009	0.496	101.9 ± 0.352	0.358
120%	99.46 ± 0.790	0.785	100.19 ± 1.93	1.93

*Average of six determinations **Table No.3:-**Result of Accuracy.

	Drug	Lable claim	Amount Found ± SD*	% Lable claim± SD*
Tablet	Montelukast sodium	10mg	10.03 ± 0.148	99.7 ± 0.597
	Olopatadine hydrochloride	5mg	5.02 ± 0.0611	100.58 ± 1.14

*Average of three determinations **Table No.4:-** Result of analysis of tablet formulation.

Formulation	Drug	Lable claim	Amount Found ± SD*	% Lable claim± SD*
Analyst 1	Montelukast sodium	10mg	9.94 ± 0.122882	99.4±1.22882
	Olopatadine hydrochloride	5mg	4.936667±0.090738	98.65667±1.5250
Analyst 2	Montelukast sodium	10mg	9.916667±0.051316	99.19667±0.527289
	Olopatadine hydrochloride	5mg	5.05±0.045826	101.0167±0.922406

*Average of three determinations **Table No.5:-** Result of Ruggedness

DISCUSSION

The montelukast sodium and olopatadine hydrochloride shows solubility in methanol. .Linearity range for montelukast sodium and olopatadine hydrochloride is 2-20µg/mL and 1-10µg/mL at respective selected wavelengths. We require to study two or more variables at a time; we study the relationship between these two or more variables. Value of coefficient of correlation always lies between -1 and +1.The coefficient of correlation for montelukast sodium at 345nm and for olopatadine hydrochloride at 206 nm is 0.9993 and 0.9992 respectively, it shows good result. Olopatadine hydrochloride and montelukast sodium shows limit of detection 0.07 µg /mL and 0.208µg /mL and limit of quantitation 0.2 µg /mL and 0.63 µg /mL respectively (See Table No.1). Precision is determined by studying the repeatability and intermediate precision. Repeatability result indicates the precision under the same operating condition over a short interval of time and interassay precision. Intermediate precision study expresses within laboratory variation in different days. In both intra and inter day precision study for both shows %RSD are not more than 2.0% which indicates good repeatability and intermediate precision. (See Table No.2).Both drugs shows good regression values at their respective wavelengths and the results of recovery study reveals that any small change in the drug concentration in the solution could be accurately determined by the proposed methods. (See Table No.3)Percentage estimation of montelukast sodium and olopatadine hydrochloride from tablet dosage form by method is 99.7% and 100.58% with standard deviation<2 (See Table No.4).

ACKNOWLEDGEMENT

The authors are thankful to Melody pharma, Mumbai and Indoco remedies, Mumbai for generous gift of pure drug sample to carry out the study and also thanks of Dr.S.K.Mohite, Vice Principal, Rajarambapu College of Pharmacy, Kasegaon for their support to carry out such a research work.

REFERENCES

1. Schoors DF, Smet MD, Reiss T, Margolskee D, Cheng H, Larson P, *et al*. ,Single dose Pharmacokinetics, safety and tolerability of MK-0476: A new leukotriene D4-receptor antagonist, in healthy volunteers. , Br J Clin Pharmacol 1995; 40:277-80.
2. Goodman, Gilman. The Pharmacological basis of Therapeutics. 10th ed: Mc Grawhill; 2001.
3. A.Avni Murat MD., T.Yavuz PhD. T.Adem MD and A. Nurettin MD., Comparison of the effect of ketotifenfumarate 0.025% and olopatadine HCl 0.1% ophthalmic solutions in seasonal allergic conjunctivitis. Clinical Therapeutics, 2005; 27:1392-1402.
4. P.Saifulla Khan, P.Janaki Pathi, P.Raveendra Reddy, V.Krishana Reddy and N.Appalaraju "Extractive Spectrophotometric estimation of Olopatadine using Acid dyes in Tablet dosage forms". Journal of Pharmacy Research, 2012; 5(4): 2104-2106.
5. Suddhasattya dey, y.vikram reddy, swetha.b, sandeep kumar. Method development and validation for the estimation of olopatadine in Bulk and pharmaceutical dosage forms and Its stress degradation studies using uv-vis Spectrophotometric method**,** International Journal of Pharmacy and Pharmaceutical sciences, 2010;2(4):212-218
6. The pharmaceutical codex, principles & practice of pharmaceutical, 12th edition, the Pharmaceutical press, London, 908.
7. Robert. A. Nash, Alfred. H. Watcher: Pharmaceutical process validation, an international third edition, revised & expanded: 507-522.

*****