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# ESTIMATION AND VALIDATION OF MONTELUKAST AND BAMBUTEROL BY CHROMATOGRAPHIC TECHNIQUES

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## ABSTRACT

A simple, specific and accurate reverse phase high performance liquid chromatographic method for the estimation of Bambuterol and Montelukast in pharmaceutical dosage form. The HPLC system consisted of Younglin (S.K.) isocratic system UV detector. Model no. Acme900. The software used was Autochro – 3000. The column used in this method $C_8$ (AGILENT). The configuration of the column is 4.6 x 250mm, particle size 5µm., with mobile phase containing Methanol: Water (0.1%Triethylamine (TEA) pH adjusted to 3.3 with dil. Orthophosphoric(OPA) acid solution. The flow rate 0.7ml/min and effluents were monitores at 225nm. The recoveries of Bambuterol and Montelukast were found to be 98.85% to 102.25% w/v and 98.08% to 102.70% w/v, respectively. The proposed method was validate and successfully applied to the estimation of Bambuterol and Montelukast in combined tablet dosage forms.

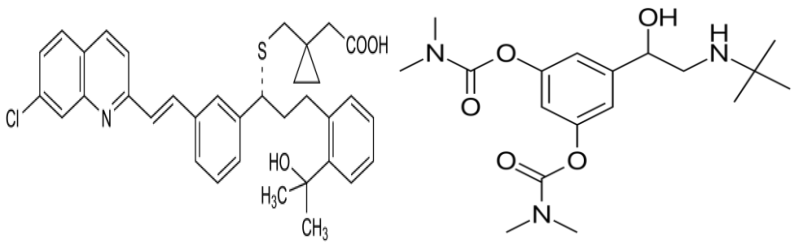
**KEYWORDS**: HPLC, Validation, Bambuterol, Montelukast.

## INTRODUCTION

Montelukast is leukotrine receptor blocker, administered orally as tablet in the dose of 5-10 mg per day. Chemically it is represented as 2-[1-({[(1r)-1-{3-[(e)-2-(7-chloroquinolin-2-yl)ehenyl]phenyl}-3-[2-(2-hydroxypropan 2yl)propyl]sulfanyl}mrthyl)cyclopropyl] acetic acid. Used in the treatment of chronic asthma and allergic rhinitis. It is not official in IP, BP and USP. Molecular weight of Montelukast is 586.184g/mol. Molecular formula is $C_{35}H_{36}CLNO_3S$. Bambuterol is a long acting beta-adrenoceptor agonist (LABA) used in the treatment of asthma. Chemically it is represented as 3-[2-(tert-butylamino)-1-hydroxyethyl]-5-[(dimethylcarbamoy)oxy]phenyl,n-dimethylcarbamate. Molecular weight of Bambuterol is

367.44 g/mol. Molecular formula of is $C_{18}H_{29}N_3O_5$. The pharmacologic effects of bambuterol are at least in part attributable to stimulation through beta-adrenergic receptors (beta 2 receptors) of intracellular adenyl cyclase, the enzyme that catalyzes the conversion of adenosine triphosphate (ATP) to cyclic AMP. Increased cyclic AMP levels are associated with relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.

**Montelukast** **Bambuterol**




## Experimental

### Instruments and Apparatus

The chromatography was performed on Younglin (S.K.) isocratic system UV detector. Model no. Acme900. The software used was Autochro – 3000. The column used in this method $C_8$ (AGILENT). The configuration of the column is 4.6 x 250mm, particle size 5µm., with mobile phase containing Methanol: Water (0.1%Triethylamine (TEA) pH adjusted to 3.3 with dil. Orthophosphoric (OPA) acid solution. The flow rate 0.7ml/min and effluents were monitores at 225nm.

### MATERIAL AND METHOD

Combination tablet formulation containing Montelukast sodium equivalent to Montelukast 10 mg and Bambuterol hydrochloride 10 mg was procured from local pharmacy. Distilled water, methanol, acetronitrile used were of HPLC grade. Stationary phase $C_8$, 5µm, column is 4.6 x 250mm was used.

### Preparation of sample solutions

50 mg of Montelukast and 50 mg of Bambuterol was weighed accurately and transferred to separate 10 ml volumetric flask, dissolved in sufficient quantity of methanol: water and diluted to 10ml with the same solvent (Methanol**:** Water, 82:18v/v) pH 3.2 with TEA to give a stock solution of 1000 ppm. The solution was sonicated for 15 min. The flask was allowed

to stand for 5 min at room temperature. The solutions were shaken vigorously for 10 min and filtered through 0.45 µg nylon membrane filters.

**Method Validation**

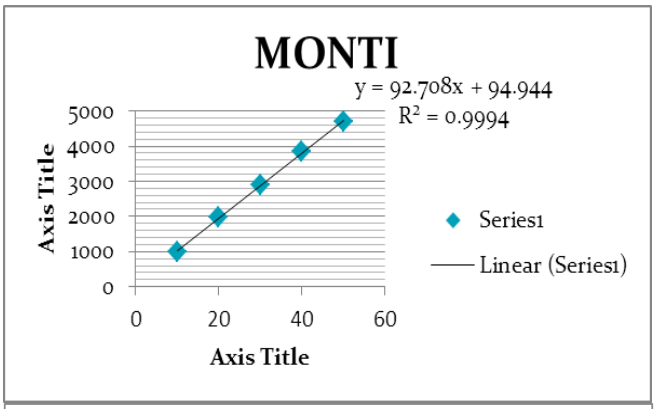
The methods were validated in compliance with ICH guidelines.

**Linearity**

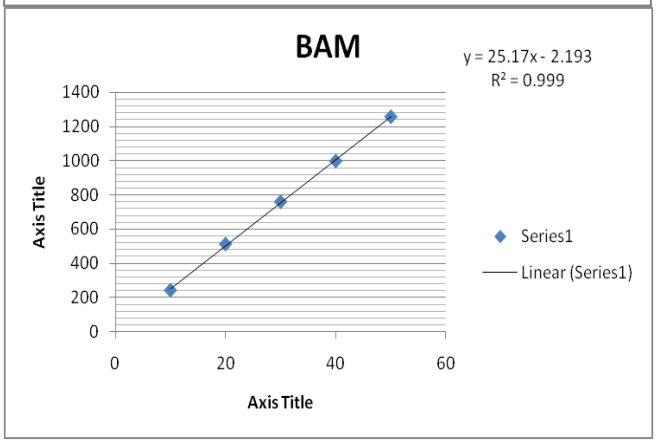
Linearity of Montelukast was observed in the range of 10-50 µg/ml and 10-50 µg/ml Bambuterol was observed in the range of 10-50 µg/ml. Detection wavelength used was 225 nm. The calibration curve yielded correlation coefficient ($r^2$) 0.999 & 0.999 for Montelukast and Bambuterol respectively.

**Linearity study**

| Sr. No. | Concentration µg/ml Bambuterol | Concentration µg/ml Montelukast | Area Bambuterol | Area Montelukast |
|---|---|---|---|---|
| 1 | 10 | 10 | 242.1801 | 976.1162 |
| 2 | 20 | 20 | 512.4691 | 1954.1152 |
| 3 | 30 | 30 | 758.8169 | 2887.9897 |
| 4 | 40 | 40 | 998.7151 | 3803.6545 |
| 5 | 50 | 50 | 1256.0237 | 4664.2466 |




| Regression Equation Data Y=mx+c | |
|---|---|
| Slope(m) | 92.70 |
| Intercept(c) | 94.94 |
| Correlation Coefficient | 0.999 |




| Regression Equation Data Y=mx+c | |
|---|---|
| Slope(m) | 25.17 |
| Intercept(c) | 2.193 |
| Correlation Coefficient | 0.999 |

**Precision**

Precision studies were carried out using parameter like intra-day and inter-day precision, the study showed that the result were within acceptance limit. i.e. % RSD below 2.0 indicating reproducibility of the method.

| Sr.no | Conc. | Area | II | Mean | Amt found | %Amt found | SD | RSD |
|---|---|---|---|---|---|---|---|---|
| 1 | 20 | 1956.34 | 1976.98 | 1966.66 | 20.19 | 100.95 | 14.59 | 0.74 |
| 2 | 30 | 2874.94 | 2888.53 | 2881.74 | 30.06 | 100.20 | 9.61 | 0.33 |
| 3 | 40 | 3807.48 | 3855.69 | 3831.59 | 40.30 | 100.75 | 34.09 | 0.89 |

| Sr.no | Conc. | Area | II | Mean | Amt found | %Amt found | SD | RSD |
|---|---|---|---|---|---|---|---|---|
| 1 | 20 | 514.95 | 518.96 | 516.96 | 20.45 | 102.25 | 2.84 | 0.55 |
| 2 | 30 | 760.86 | 758.84 | 759.85 | 30.10 | 100.33 | 1.43 | 0.19 |
| 3 | 40 | 999.67 | 995.52 | 997.60 | 39.54 | 98.85 | 2.93 | 0.29 |

**Recovery studies**

Accuracy of method is ascertained by recovery studies performed at different levels of concentrations (80%, 100% and 120%). The % recovery was found to be within 99-101%.

| Level of Recovery (%) | Drug | Mean % Recovery | Standerd Deviation* | %RSD |
|---|---|---|---|---|
| 80 | BAMBUTEROL | 103.34 | 1.64 | 1.59 |
| | MONTELUKAST | 103.3 | 0.71 | 0.70 |
| 100 | BAMBUTEROL | 102.78 | 0.81 | 0.78 |
| | MONTELUKAST | 100.81 | 0.16 | 0.16 |
| 120 | BAMBUTEROL | 101.58 | 0.24 | 0.24 |
| | MONTELUKAST | 101.58 | 0.11 | 0.10 |

***Denotes average of three determinations.**

**System suitability test**

Syatem suitability was performed to verify, wether the resolution and reproducibility of the chromatographic system are adequate.

| System Suitability Parameters | Proposed Method | |
|---|---|---|
| | BAMBUTEROL | MONTELUKAST |
| Retention Time | 3.5500 | 6.5167 |
| Area | 747.8178 | 2894.4573 |
| Theoretical Plate Number | 5134 | 8477.6 |
| Taling Factor | 1.0714 | 1.1111 |

**Robustness**

To evaluate the robustness of the method, the parameters selected were varied at three levels. The results indicate that less variability in retention time and tailing factor were observed.

**Result of Robustness Study of Montelukast**

| Parameters | Conc. | Amount of detected (mean ±SD) | % RSD |
|---|---|---|---|
| Mobile phase composition-(91+9) | 30 | 20.80±0.09 | 0.71 |
| Mobile phase composition-( 89+11) | 30 | 20.74±0.67 | 0.71 |
| Wavelength change224nm | 30 | 4.52±0.89 | 0.17 |
| Wavelength Change 226nm | 30 | 5.23 ± 0.86 | 0.18 |
| Flow rate change(0.6ml) | 30 | 14.46± 0.71 | 0.43 |
| Flow rate change(0.8ml) | 30 | 27.68 ± 0.54 | 1.13 |

**Result of Robustness Study of Bambuterol**

| Parameters | Conc. | Amount of detected (mean ±SD) | % RSD |
|---|---|---|---|
| Mobile phase composition-(91+9) | 30 | 1.36±0.92 | 0.19 |
| Mobile phase composition-( 89+11) | 30 | 1.37±0.67 | 0.19 |
| Wavelength change224nm | 30 | 4.34±0.89 | 0.52 |
| Wavelength Change 226nm | 30 | 1.86± 1.82 | 0.24 |
| Flow rate change(0.6ml) | 30 | 1.38± 1.48 | 0.16 |
| Flow rate change(0.8ml) | 30 | 1.49± 0.97 | 0.24 |

**DISCUSSION**

The analysis of tablet formulation was done and the results obtained within the limits. The results obtained for validation study were within the limit specified by the ICH guidelines and hence the method was found to be linear, precise. The results of recovery study were within ICH limits, thus indicating the accuracy of method.