# Stability Indicating Method Development and Validation for Determination of Metoprolol Succinate (MLS) by using RP-HPLC method in Pharmaceutical Dosage Form

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*Abstract*—**Metoprolol Succinate (MLS) belongs to the class of compounds known as β-adrenergic antagonists. The chemical structure of metoprolol consists of substituted phenylpropanolamine, providing the necessary structural features for selective β-1 adrenergic receptor blockade. As one of the first selective β blockers, metoprolol mainly affects the β-1 receptors in the heart and less affects the β-2 receptors in the lungs and blood vessels. Metoprolol was patented in 1970 and approved for medical use in 1978. Metoprolol is now a generic medication under various brand names, such as Lopressor, Toprol-XL, and Betaloc. The study aims for the development and validation of a reverse phase high-performance liquid chromatography (RP-HPLC) method for Metoprolol Succinate in pharmaceutical dosage forms is crucial for quality control in drug manufacturing. The primary aim is to establish a reliable analytical methodology that accurately quantifies both active pharmaceutical ingredients in a single run, enhancing efficiency and reducing costs. This research supports pharmaceutical quality assurance practices and compliance with regulatory requirements. In this study, we found that the pharmaceutical dose tablet formulations containing Metoprolol Succinate (MLS) may be accurately measured using the RP-HPLC method. The RP-HPLC technique is sensitive, accurate, precise, and repeatable; it also demonstrates high repeatability. Metoprolol Succinate (MLS) tablet dosage formulation analysis may also be conducted with success. These techniques do not experience any influence from additives, matrices, etc. To further understand these trials, additional research on other medication formulations is needed.**

*Index Terms*—**Metoprolol Succinate; RP-HPLC; Lopressor; Pharmaceutical Dosage Form.**

## 1. INTRODUCTION

Metoprolol (Figure 1) belongs to the class of compounds known as β-adrenergic antagonists. The chemical structure of metoprolol consists of substituted phenylpropanolamine, providing the necessary structural features for selective β-1 adrenergic receptor blockade. As one of the first selective β blockers, metoprolol mainly affects the β-1 receptors in the heart and less affects the β-2 receptors in the lungs and blood vessels. Metoprolol was patented in 1970 and approved for medical use in 1978. Metoprolol is now a generic medication under various brand names, such as Lopressor, Toprol-XL, and Betaloc (1-5).

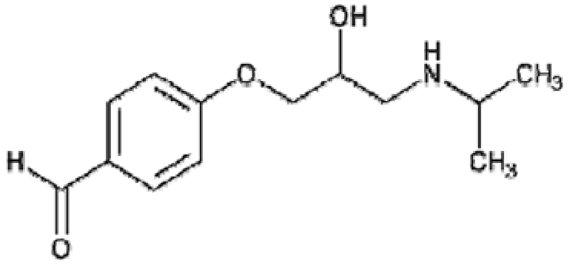

Figure 1: Metoprolol

The study aims for the development and validation of a reverse phase high-performance liquid chromatography (RP-HPLC) method for Metoprolol Succinate in pharmaceutical dosage forms is crucial for quality control in drug manufacturing. The primary aim is to establish a reliable analytical methodology that accurately quantifies both active pharmaceutical ingredients in a single run, enhancing efficiency and reducing costs. This research supports pharmaceutical quality assurance practices and compliance with regulatory requirements.

## 2. MATERIALS AND METHODS

### 2.1 Procurement of the Drug

Metoprolol Succinate (MLS), a medication from Arch Pharma labs Ltd Thane, is available in a 10g package with a purity of 99.8 to be used as Reference drug while Lopressor which contains 25 mg dosage of Metoprolol Succinate to be used as test drug.

### 2.2 Method and Procedure

### 2.2.1 Selection of Mobile Phase

The mobile phases tested include methanol: water (90:10), methanol: water (80:20), acetonitrile: water (90:10), acetonitrile: phosphate buffer 10mm (90:10), acetonitrile: phosphate buffer 10mm (80:20), and acetonitrile: phosphate buffer (75:25) with pH 4.5.

### 2.2.2 Chromatographic Conditions

The chromatographic conditions were established through trial and error, maintaining constant consistency throughout the method. The column was Inertsil 4.6 x 250 mm, with a particle size of 5 µm, stationary phases of C18 Inertsil, mobile phase of Acetonitrile: Phosphate Buffer (75:25), pH 4.5, and a sample size of 20 µL.

### 2.2.3 Validation of the Method

Adjusting several UFLC settings (FDA, 1995, 1997, 2000, 1994, 1987; USP, 2000) confirmed the reliability of the UFLC approach (6). Calibration plot least-squares linear regression analysis verified the UFLC method's linearity (7), the limits of detection and quantification for the medicines mentioned were determined to be three and five epochs, respectively, above and below the baseline noise, The process adhered to the guidelines established by the United States Pharmacopoeia (USP, 2000), specificity (7), precision (8) accuracy (9), robustness (10) and ruggedness (11, 12) were determined..

## 3. RESULTS AND DISCUSSION

### 3.1 Selection of the Mobile Phase

From various mobile phases tried, mobile phase containing Acetonitrile: Phosphate Buffer (80:20) pH 4.5 was selected, since it gives sharp reproducible retention time for MLS (Figure 1).

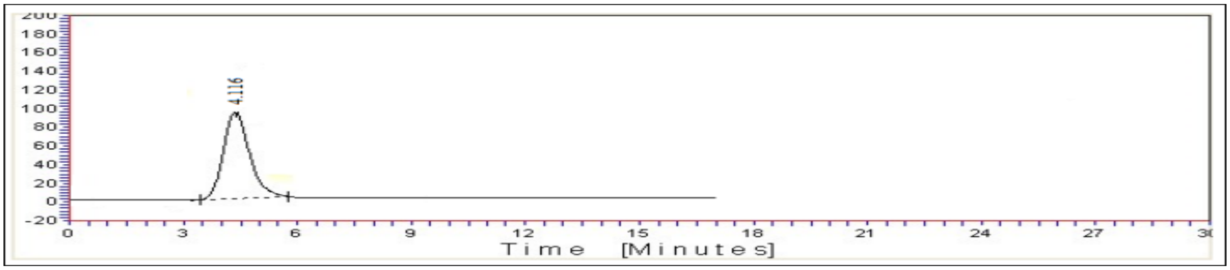

Figure 1: Trial Chromatogram obtained by using Acetonitrile: Phosphate Buffer10mm (80:20) pH4.5 as mobile phase of MLS

### 3.2 Validation of the Method

Accuracy was determined by recovery trials conducted using the conventional addition method (Table 1).

Table 1: Results and Statistical Data for Recovery study of MLS

| Sr. No | wt. of formulation | Amount of Drug Added in (µg/ml) | eak Area of stand. | Peak Area of sample | % Recovery |
|---|---|---|---|---|---|
| | MLS | MLS | MLS | MLS | MLS |
| 1 | 105.16 | 1.00 | 63548.2 | 63522.4 | 99.4 |
| 2 | | 1.25 | | 63542.3 | 99.8 |
| 3 | | 1.50 | | 63579.8 | 99.7 |
| 4 | | 2.00 | | 63517.3 | 99.6 |
| 5 | | 2.25 | | 63066.9 | 100.8 |
| 6 | | 2.50 | | 63029.4 | 100.9 |
| 7 | | 3.00 | | 63154.3 | 101.1 |
| 8 | | 3.25 | | 63404.2 | 101.5 |

| | | | | | |
|---|---|---|---|---|---|
| 9 | | 3.50 | | 62999.1 | 100.2 |
| | | | | Mean | 100.42 |
| | | | | S.D. | 0.815 |

The precision of an analytical approach is denoted by the standard deviation (S.D.) or relative standard deviation (R.S.D.) of a sequence of observations. The medicines were quantified using replicate estimate using the suggested approach (Table 2).

Table 2: Results and Statistical Data of Precision Study

| Sr. No. | Weight of Standard (mg) | Weight of Sample (mg) | Peak Area of Stand. | Peak Area of Sample | % Label claim |
|---|---|---|---|---|---|
| | MLS | MLS | MLS | MLS | MLS |
| 1 | 15.16 | 105.15 | 63548.2 | 63404.7 | 99.90 |
| 2 | | 105.99 | | 62929.7 | 99.19 |
| 3 | | 105.79 | | 63217.3 | 99.60 |
| | | | | Mean | 99.99 |
| | | | | ±S.D. | 0.252 |

Specificity was assessed by the suggested method's capacity to achieve well-separated peaks for MLS without interference from matrix components. Mean retention time for MLS is 3.981. The results obtained closely aligned with those in the typical laboratory combination, indicating no influence from the matrix components. In accordance with USP guidelines, tablet powder corresponding to 80%, 90%, 100%, 110%, and 120% of the label claim was extracted and subsequently dissolved and diluted with the mobile phase to achieve a concentration within the range of 80% to 120% of the test concentration. The chromatograms of the resultant solutions were recorded. The commercial formulation of MLS demonstrated linearity within ± 20% of the test concentration for the corresponding medication (Table 3s).

Table 3: Observations of Linearity and range study for MLS

| Sr. No. | % Label claim | Peak area |
|---|---|---|
| 1 | 80 | 50973.09 |
| 2 | 90 | 66220.95 |
| 3 | 100 | 63367.15 |
| 4 | 110 | 70713.92 |
| 5 | 120 | 75060.69 |

The robustness research demonstrated that the chosen parameters were invariant to minor fluctuations in the organic content of the mobile phase, wavelength, and flow rate. The system suitability findings must fall within the specified limits. Therefore, the approach was resilient. The limit of detection is the minimal quantity of analyte in a sample that can be identified, albeit not necessarily quantified as a precise value. The limit of quantitation is the minimum concentration of analyte in a sample that can be quantitatively measured with appropriate precision and accuracy (Table 4). Upon setting the chromatographic conditions, a standard laboratory mixture was generated and analysed according to the technique outlined in the experimental and results sections. It provided precise, dependable findings and was adapted for the quantification of pharmaceuticals in commercial tablet formulations.

Table 4: Limit of detection (LOD) and Limit of Quantization (LOQ)

| Sr. No. | Drug Name | LOD (□g/ml) | LOQ (□g/ml) |
|---|---|---|---|
| 1 | MLS | 0.030 | 1.111 |

## 4. CONCLUSIONS

In this study, we found that the pharmaceutical dose tablet formulations containing Metoprolol Succinate (MLS) may be accurately measured using the RP-HPLC method. The RP-HPLC technique is sensitive, accurate, precise, and repeatable; it also demonstrates high repeatability. Metoprolol Succinate (MLS) tablet dosage formulation analysis may also be conducted with success. These techniques do not experience any influence from additives, matrices, etc. To further understand these trials, additional research on other medication formulations is needed.

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