# ANALYTICAL METHOD VALIDATION PROTOCOL CUM REPORT FOR RESIDUAL SOLVENT OF LEVOCETIRIZINE & MONTELUKAST TABLETS

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|---|---|---|
| **Name of the Product** | **:** | LEVOCETIRIZINE & MONTELUKAST TABLETS |
| **Department** | **:** | QUALITY CONTROL |
| **Protocol No.** | **:** | |
| **Effective Date** | **:** | |

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## 1. PRE APPROVAL:

Document is Prepared, Reviewed and Approved by the following persons for Pre Approvals.

**Prepared By :**

| Department | Name | Designation | Signature/ Date |
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| Quality Control | | | |

**Reviewed By:**

| Department | Name | Designation | Signature/ Date |
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| Quality Assurance | | | |

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# ANALYTICAL METHOD VALIDATION OF RESIDUAL SOLVENT OF LEVOCETIRIZINE & MONTELUKAST TABLETS

2. **OBJECTIVE:** The objective of this protocol cum report is to establish a documented evidence for the Residual Solvent Method Validation of Levocetirizine & Montelukast Tablets.

3. **SCOPE:** This Protocol cum report is applicable for Residual Solvent test of Levocetirizine & Montelukast Tablets for Specificity and Precision, domestic market in Quality Control Department.

4. **RESPONSIBILITY:** Officer/Executive-QC is responsible for the preparation of the protocol. The protocol shall be reviewed / approved by the Officer/Executive/Manager –QC/QA, approved by Head QA/QC.

5. **REFERENCES:**

SOP: Operation and calibration of GC.
SOP: Procedure Validation Activities.
SOP: Operation and calibration of analytical balance.
SOP: Procedure for handling of reference/working standard.
SOP: Handling procedure of Gas chromatography column

6. **METHODOLOGY:**

**RESIDUAL SOLVENT (BY GC):**

**Equipment /Instrument Required:**

- Gas Chromatography
- Analytical Balance
- Calculator

**Glass wares required:**

- Volumetric Flask
- Beaker

**Chromatographic conditions:**

Column : A 0.53 mm x 30 m, 3.0µm fused-silica analytical column coated with 6% Cyanopropyl-phenyl 94% dimethylpolysiloxane (DB-624)

Detector : Flame-ionization detector

Carrier gas : Nitrogen

Flow rate : A Flow of about 2ml/minute

Make-up gas : Nitrogen, if recommended

Injection port temperature: 210°C

Detector temperature : 260°C

Column temperature : Programmed according to the following steps.

It is maintained at 40° C for 10 minutes, and then increased to 230°C at a rate of 30°C per minute, and hold for 5 minutes.

**Head space parameter:**

Vial incubation temperature: 90°C

Vial incubation time : 20 minutes

Transfer line temperature: 110°C

Syringe temperature : 100°C

Carrier gas : Nitrogen

Pressurization time : 2.0 minutes

Injection volume : 0.1 ml

Withdrawal time : 0.5 minutes

Carrier pressure : 15 psi

Split ratio : 2:1

**Standard preparation:** Prepare a solution, in DMSO. Dissolve 60 mg of Dichloromethane and 500 mg IPA and dilute to 100 ml with DMSO. Further dilute 10 ml of this solution to 100 ml with DMSO. [Note: Prepare fresh standard for daily use]

**Test preparation:** Take 20 tablets and crush to fine powder. Weigh 1.0 g of sample in 20 ml Headspace vial, add 5 ml of DMSO.

**Procedure:** Take 5 ml of standard solution in 6 different 20 ml headspace vial, Separately inject equal volumes of Blank (DMSO), Standard solution (Six injections) and sample solution (Duplicate) into the system, record the chromatogram and measure the peak responses. The relative standard deviation of the Dichloromethane (MDC) and Isopropyl alcohol (IPA) peak response from replicate injections is not more than 15%. Order of elution is MDC and IPA.

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**System suitability:** The resolution between each peak more than 1.5 and percentage relative standard deviation for six replicate of standard is not more than 15%.

**Calculation:**

**Dichloromethane in µg per g:**

$$\text{Content in ppm} = \frac{At}{As} \times \frac{Ws}{100} \times \frac{10}{100} \times \frac{5}{Wt} \times \frac{P}{100} \times 1000000$$

Where,

At : Average area of the peak due to Dichloromethane in test preparation.

As : Average area of the peak due to Dichloromethane in standard preparation.

Ws : Weight of Dichloromethane working standard taken, in mg.

Wt : Weight of sample taken, in mg.

P : Potency of Dichloromethane working standard.

**Isopropyl Alcohol in µg per g:**

$$\text{Content in ppm} = \frac{At}{As} \times \frac{Ws}{100} \times \frac{10}{100} \times \frac{5}{Wt} \times \frac{P}{100} \times 1000000$$

Where,

At : Average area of the peak due to Isopropyl Alcohol in test preparation.

As : Average area of the peak due to Isopropyl Alcohol in standard preparation.

Ws : Weight of Isopropyl Alcohol working standard taken, in mg.

Wt : Weight of sample taken, in mg.

P : Potency of Isopropyl Alcohol working standard.

**6.1 SPECIFICITY:**

The specificity of an analytical method is its ability to measure unequivocally the analyte in the presence of components that may be expected to be present in the test matrix**.**

**Note:** For detailed of procedure, refer methodology

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| S.No. | Validation parameters | Acceptance Criteria | Observation | |
|---|---|---|---|---|
| 1 | **Specificity** | There should be no interference observed from Blank, mix Standard and sample to the Dichloromethane, Isopropyl Alcohol | Name of Analyte | RT |
| | | | Dichloromethane | -- |
| | | | Isopropyl Alcohol | 5.098 |
| | | | No Interference observed from Blank, Mixed Standard and Sample | |

## 6.2 PRECISION:

| | | | | | |
|---|---|---|---|---|---|
| 2 | **Precision** | System Precision | The %relative standard deviation (% RSD) of the peak areas for Dichloromethane, Isopropyl Alcohol must not be more than 15.0%. | **Name of Analyte** | |
| | | | | Dichloromethane | |
| | | | | Isopropyl Alcohol | |
| | | Method Precision | The Result of Test must comply with the Specification. | **Name of Analyte** | **Area of Test** |
| | | | | Dichloromethane | Not detected |
| | | | | Isopropyl Alcohol | 22942602 |