# FORMULATION, OPTIMIZATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF MONTELUKAST SODIUM

Saurabh Bhardwaj*[1], Pranshu Tangri [1] and Dr. Preeti Kothiyal [1]
Division of Pharmaceutical Sciences,
Shri Guru Ram Rai Institute of Technology & Science, Dehradun, India

## ABSTRACT

Mouth Dissolving Tablets are also known as quick dissolves, Mouth melts, Mouth dissolving, Mouth disintegrating, rapid-dissolve, or orally dissolving tablets. Their characteristic advantages such as administration, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market. The aim of this article is to review the progress of the evolving technologies and super disintegrating agents in the formulation, manufacturing and evaluation of these tablets. Montelukast sodium tablets prepared by wet granulation method using croscarmellose sodium, sodium starch glycolate (Primogel) as superdisinteganting agents, Further preformulation studies were performed for proper selection of preparation technique, compatibility studies were carried out for selecting excipient and co-formulating agents prepared model API. Hardness, in vitro disintegration time, friability, interaction studies etc. in vitro evaluation of tablet prepared was also carried out. It can be concluded that mouth dissolving tablet prepared from croscarmellose sodium and sodium starch glycolate (Primogel) have much better in vitro dissolution as compared with tablet compared with tablet prepared from Crospovidone XL-10 and Sodium starch glycolate. The hardness test indicates well mechanical strength. The hardness of all tablets was found to be **1.5- 3.8 (kg/cm$^2$),** Friability of formulation was found to be less than **1 %,** which shows the tablet has well mechanical resistance. Drug content was found to be – **99.75 %** of final formulation and similarly in all formulations. The in vitro disintegration time was found to be **47 seconds** of final formulation (F-8). The in vitro release time of final formulation of montelukast sodium was found to be **99.62 %** in 18 minutes.

**Key words:** Montelukast sodium, Formulation, Optimization and Evaluation.

## INTRODUCTION

Many patient groups, such as the elderly, children, mentally retarded, uncooperative or nauseated, have difficulty in swallowing conventional dosage forms, like tablets. Swallowing conventional tablets will be further hindered by conditions such as unavailability of water, allergic reactions and episodes of coughing. These problems can be solved by developing rapidly disintegrating and dissolving tablet dosage forms for oral administration, because they dissolve in saliva and does not require water for swallowing. Upon ingestion, the saliva serves to rapidly dissolve the dosage form. The saliva containing the dissolved or dispersed medicament is then swallowed and the drug is absorbed in the normal way. Some drugs are

absorbed from the mouth, pharynx and oesophagus, as the saliva passes down in to the stomach. In these cases, the bioavailability of drugs is significantly greater than those observed from conventional dosage forms. The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablets. A wide range of drugs requiring quick onset of action are the promising candidates for this dosage form. These include neuroleptics, antidepressants, cardiovascular drugs, analgesics and so on. Mouth dissolving tablets (MDTs) can be prepared by different methods, such as direct compression, freeze-drying, spray drying, sublimation, wet granulation method. The basic approach for the development of MDTs is the use of superdisintegrants. The aim of this study was to formulate MDTs with sufficient mechanical integrity and to achieve faster disintegration in the oral cavity without water. To achieve this goal, mannitol used as diluent and aspartame as sweetening agent for the formulation of tablets. Attempts were made to enhance dissolution rate along with faster disintegration using superdisintegrants, like croscarmellose sodium, sodium starch glycolate and crospovidone. Montelukast sodium was selected as the active pharmaceutical ingredient in the study.

## MATERIALS AND METHODS

Montelukast sodium was a gift from Wang Pharmaceutical & Chemicals. Croscarmellose sodium used was analytical reagent grade procured from SCOP Ingredients Pvt. Ltd., and Sodium Starch Glycolate used was procured from PIOMA Chemicals Pvt. Ltd. All other reagents and chemicals used were of analytical grade.

## METHODOLOGY

### Pre-Formulation Study

Pre-Formulation Study is the initial phase in the discerning improvement of dose type of a medication substance. The goal of preformulation examines is to build up an arrangement of the data about the medication substance, with the goal that this data is valuable to create plan. Preformulation can be characterized as examination of physical and synthetic properties of medication substance and when joined with excipients. Preformulation examinations are outlined those physiochemical properties and excipients that may impact the definition plan, technique for fabricate, and pharmacokinetic-biopharmaceutical properties of coming about item. Following are the test preformed for Preformulation considers which included similarity ponders, organoleptic properties assurance of dissolving point, assurance of solvency studies and assurance of Partition coefficients.

1. **Procurement of the materials for the research work:** Montelukast Sodium is selected for the project work. Cross carmelose Sodium and Sodium Starch Glycolate are selected as Super

Disintegration Agent and Aspartame is selected as sweetening Agent and Magnesium Stearate selected for Lubrication purpose.

2. **Determination of Melting point:** The drug will be filled in one end fused Capillary tube and kept into digital melting point apparatus. The apparatus will operated and the temperature at which drug will start melting will be noted as melting point (IP 2010).
3. **Determination of functional groups by FTIR** KBr discs will be prepared by means of hydrostatic pressure of 6-8 tons using KBr press. Then FTIR spectra will be recorded between scanning ranges of 400-4000 cm. (IP 2010).
4. **Drug – Excipients Compatibility study:-**The Primary objective of this investigation was to identify a stable storage condition for drug in solid and identification of compatibility excipients for its information. This can be confirmed by carrying out by infrared light absorption scanning spectroscopy (IR) studies. Pure drug, Excipients and KBr were mixed in a ratio of 1:3, and in the form of pellets, infra-red spectra of pure drug and mixture of formulation were recorded by dispersion of drug and mixture of formulation in KBr using Fourier infrared Spectrophotometer. A base line correlation was made using dried potassium bromide and then the spectra of the dried mixture of drug, formulation mixture and potassium bromide were recorded on FTIR.
5. **Determine the Solubility:** The solubility determination of Montelukast Sodium was carried out in water, ethanol and Methanol and Chloroform. The excess drug was added gradually to 10 ml of each solvent contained in beaker and beaker was sealed with aluminium seals. The solution were shaken and allowed to equilibrate for 24 hrs. Undisturbed. The solutions containing excess of drug were centrifuged for 5 minutes in ultra-centrifuge and filtered through Whatsman filters. Filtrate was analyzed on UV-Visible spectrophotometer.

**Table No.1.1 Determination of Solubility: - (IP-2010)**

| S.NO. | TERM | Part of Solvent Required To Dissolve 1 Part of Solute |
|---|---|---|
| **1.** | Very Soluble | Less Than 1 Part |
| **2.** | Freely Soluble | 1-10 Part |
| **3.** | Soluble | 10-30 Part |
| **4.** | Sparingly Soluble | 30-100 Part |
| **5.** | Slightly Soluble | 100-1000 Part |

| | | |
|---|---|---|
| **6.** | Very Slightly Soluble | 1000-10,000 Part |
| **7.** | Practically Soluble | More Than 10,000 part |

**6. Determination of Partition Coefficient:-**

The partition coefficient of Montelukast Sodium in Water was determined by using equal amount of n-octanol as an oil phase and Water as the Aqueous phase. In a separating funnel these two phases were mixed in equal quantities.in solvent system required quantity of drug was mixed then the mixture was shaking by hand shaking method until equilibrium was achieved. After that separating funnel kept aside for 20 mins after this 20 mins aqueous phase was filtered and 1 ml of this phases was taken and diluted with Water and measured the absorbance of Montelukast Sodium l in aqueous phase at 345 nm using UV-Spectrophotometer. the partition coefficient of Montelukast Sodium was calculated by using formula.

$$P_{o/w} = (C_{oil} / C_{water})_{equilibrium}$$

## ANALYICAL METHODS:

**Determine The wavelength ($\lambda_{max}$) in different media**

1. **Determination The wavelength ($\lambda_{max}$) of Montelukast Sodium in Water ($H_2O$)**
   Standard stock solution of Montelukast Sodium will be prepared by dissolving 50 mg of Montelukast Sodium in 50 ml of Water ($H_2O$) and sonicated for 15 minutes in bath Sonicator and prepare dilution of 1 mg/1 ml i.e. 1000 µg/ml ( 1000 ppm) stock solution. From this stock solution we can 10 ppm solution .There will be scanned the drug at their standard $\lambda_{max}$ and Determine the wavelength of Montelukast Sodium.

2. **Determination The wavelength ($\lambda_{max}$) of Montelukast Sodium in Methanol**
   Standard stock solution of Montelukast Sodium will be prepared by dissolving 50 mg of Montelukast Sodium in 50 ml of Methanol and sonicated for 15 minutes in bath Sonicator and prepare dilution of 1 mg/1 ml i.e. 1000 µg/ml (1000 ppm) stock solution. From this stock solution we can 10 ppm solution .There will be scanned the drug at their standard $\lambda_{max}$ and Determine the wavelength of Montelukast Sodium.

**Preparation of Standard Plot of Montelukast Sodium in Different Media**

1. **Determination The Standard Plot of Montelukast Sodium in Water ($H_2O$)**

   Standard stock solution of Montelukast Sodium will be prepared by dissolving 50 mg of Montelukast Sodium in 50 ml of Water ($H_2O$) and sonicated for 15 minutes in bath Sonicator and prepare dilution of 1 mg/1 ml i.e. 1000 µg/ml (1000 ppm) stock solution. From this stock solution we can prepare 5-15 ppm solution .There will be scanned the drug at their standard $\lambda_{max}$ and prepared standard plot of Montelukast Sodium.

2. **Determination The Standard Plot of Montelukast Sodium in Methanol ($CH_3OH$)**

   Standard stock solution of Montelukast Sodium will be prepared by dissolving 50 mg of Montelukast Sodium in 50 ml of Methanol and sonicated for 15 minutes in bath Sonicator and prepare dilution of 1 mg/1 ml i.e. 1000 µg/ml (1000 ppm) stock solution. From this stock solution we can prepare 5-15 ppm solution .There will be scanned the drug at their standard $\lambda_{max}$ and prepared standard plot of Montelukast Sodium.

**Preparation of Mouth Dissolving Tablets of Montelukast Sodium**

In this study the mouth dissolving tablets of Montelukast sodium **(5mg)** was prepared by direct compression and wet granulation methods. Superdisintegrants (Sodium starch glycolate, crospovidone, croscarmellose sodium) were used in different concentration and ratio in each formulations.9 formulations of Montelukast sodium was prepared. Aspartame was used as main sweetener. the preparation of mouth dissolving tablets as well as following. For formulation 1 and 2, all ingredients were pass throw # 60 mesh screen separately. The drug, superdisintegrants and diluents were mixed in small proportion each time and blending it to form uniform mixture and set aside. The other ingredients were weighted and mixed in geometrical order. The 200 mg were formulated by direct compression technique using 10 station tablet punching machine.similarily for other formulations all ingredients of granulation part were passed throw # 60 and active material passed throw # 100 mesh size and mixed well to each other. After well mixing add binder and done the granulation procedure. And keep the granulation part at 40º c temperature in tray dryer. After well drying pass throw # 20 mesh size and now mixing the lubrication part in it.. the lubrication part pass throw # 60 and then mixed in the granulation part. After well mixing all materials the tablets weighing 200 mg were formulate by using the 10 station punching machine, used the 7.5mm punch for compressed 200 mg tablet weight.

**Tablet No 1.2: - Formula for mouth dissolves tablets of montelukast sodium with different concentration of superdisintegrant.**

| INGREDIENTs | FORMULATION CODE | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F-1 | F-2 | F-3 | F-4 | F-5 | F-6 | F-7 | F-8 | F-9 |
| Montelukast Sodium | 5.23 | 5.23 | 5.23 | 5.23 | 5.23 | 5.23 | 5.23 | 5.23 | 5.23 |
| DCP- Anhydrous | 84.77 | 99.0 | 97.27 | - | - | - | - | - | - |
| Croscarmellose Sod. | 5.0 | 6.0 | 6.0 | 5.0 | - | 6.0 | 4.0 | 6.0 | 6.0 |
| Sod. Starch glycolate | 6.0 | 5.0 | 5.0 | 5.0 | 6.0 | 6.0 | 8.0 | 8.0 | 8.0 |
| Crospovidone XL-10 | - | - | - | - | 6.0 | - | - | - | - |
| Mannitol (Plain) | - | - | - | 80.0 | 86.0 | 66.0 | 69.57 | 70.0 | 70.0 |
| Micro crystalline cellulose (PH-102) | - | - | - | - | - | 50.0 | 60.0 | 50.0 | 60.0 |
| Polyvinyl Pyrolodine (PVPK-30) | - | - | 2.0 | 2.0 | 2.5 | 3.0 | 3.5 | 4.0 | 4.0 |
| Isopropyl Alcohol | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |
| Orange flavor 2100 | 5.0 | 5.0 | 5.0 | 5.5 | 5.5 | 6.0 | 5.5 | 6.0 | 6.0 |
| Colloidal $SiO_2$ | 1.0 | 1.5 | 1.5 | 1.5 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Magnesium Stearate | 1.0 | 1.5 | 1.5 | 2.0 | 2.0 | 2.0 | 2.5 | 2.0 | 2.0 |
| Mannitol (Mannogen) | 90.0 | 74.27 | 70.0 | 86.27 | 76.07 | 44.07 | 30.0 | 36.57 | 26.57 |
| Citric Acid anhydrous | - | - | 4.0 | 3.5 | 4.0 | 5.0 | 4.5 | 4.0 | 4.0 |
| Aspartame | 2.0 | 2.5 | 2.5 | 3.0 | 3.5 | 4.0 | 3.0 | 4.0 | 4.0 |
| Talc | - | - | - | 1.0 | 1.0 | 1.5 | 2.0 | 2.0 | 2.0 |
| Sunset yellow lake | - | - | - | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| TOTAL (Mg) | **200.0** | **200.0** | **200.0** | **200.0** | **200.0** | **200.0** | **200.0** | **200.0** | **200.0** |

**Bioequivalent Factor of Montelukast Sodium: -**

Bioequivalence is a term in pharmacokinetics used to assess the expected in vivo biological equivalence of two proprietary preparations of a drug. If two products are said to be bioequivalent it means that they would be expected to be, for all intents and purposes the same. The bioequivalent factor of Montelukast Sodium is given as well as following;

Bioequivalent Factor of Montelukast Sodium,

$$\textbf{Standard Quantity} = \frac{\textbf{Molecular weight of Montelukast Sodium}}{\textbf{Molecular weight of Montelukast}} \times \textbf{Claim (Tab.)}$$

$$\text{Standard Quantity} = \frac{608.18}{585.19} \times 5.0 \text{ mg}$$

$$= 5.196 \text{ mg}$$

**Weight Each Table According to the % Assay and loss on Drying: -**

$$\textbf{Assay on Such Basis} = \frac{\textbf{Assay on Dried Basis } (\textbf{100} - \textbf{LOD})}{\textbf{100}}$$

$$\text{Assay on Such Basis} = \frac{99.0\ (100 - 0.63)}{100}$$

$$= 99.38 \text{ \% w/w}$$

$$\textbf{Active mterial Quantity} = \frac{\textbf{Standard Quantity (Claim)}}{\textbf{Assay on Such Basis}} \times \textbf{100}$$

$$\text{Active material Quantity} = \frac{5.196 \times 100}{99.38}$$

**Active material Quantity for each Tablet = 5.23 mg /Tablet**

**Note: - Montelukast sodium (5.23mg) is Equivalent to 5.0 mg of Montelukast.**

**Evaluation Parameters of Mouth Dissolving Tablets of Montelukast Sodium: -**

The evaluation parameters of mouth dissolving tablets of montelukast sodium given as well as following;

1. **Weight Variation Test:**

The weight of the tablet will be measured to ensure that a tablet contains the proper amount of drug. The USP weight variation test will do by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average.

**Table No. 1.3: - Weight variation specification as per I.P.**

| S.NO. | Average Weight of Tablet | % Deviation |
|---|---|---|
| **1.** | 80 mg or less | ±10 |
| **2.** | More than 80 mg but less than 250 mg | ±7.5 |
| **3.** | 250 mg or more | ±5.0 |

2. **Hardness:**

The Monsanto hardness tester will be used to determine the tablet hardness. The tablet will held between a fixed and moving jaw. Scale was adjusted to zero; load was gradually increases until the tablet will fracture. The value of the load at that point gives a measure of hardness of the tablet. Hardness was expressed in $Kg/cm^2$.

3. **Friability: -** Tablet strength will be tested by Friabilator (Electro lab India). Pre weighed tablets will allowed for 100 revolutions (4min), take out and will deducted. The percentage weight loss will calculated by rewriting the tablets. The % friability will then calculate by following equation.

$$F = \frac{(W_{initial}) - (W_{final})}{(W_{intial})} \times 100$$

**4. Thickness and Diameter:**

Control of physical dimension of the tablet such as thickness and diameter is essential for consumer acceptance and tablet uniformity. The thickness and diameter of the tablet will be measured using Vernier calipers. It will measure in mm.

**5. Determination of Flow Properties**

Flow properties of drug -loaded beads can be assessed by measuring its Carr's index and Hausner ratio. Carr's index and the closely related Hausner ratio have become the simple, fast, and popular methods of predicting flow characteristics. The Carr's index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content and cohesiveness of materials because all of these can influence the observed Carr's index. Carr's index and Hausner ratio are determined by measuring both the bulk volume and the tapped volume of a powder.

The bulk and tapped densities were measured in a 100 ml graduated measuring cylinder. The sample contained in the measuring cylinder was placed in a USP-I tap density test apparatus. At first, 100 taps were applied, and the tapped volume was noted. The tapped volume was measured once again following additional 100 taps. From the initial bulk volume and final tapped volume, respective densities were calculated.

**Carr's index was determined by the following formula.**

$$\text{Carr's Index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \text{ x100}$$

**Hausner ratio was determined by the following formula:**

$$\text{Hausner Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

**Table No. 1.4: - Scale of Flow Ability**

| S. No. | Flow Character | Carr's Index | Hausner ratio |
|---|---|---|---|
| **1.** | Excellent | 10 | 1.00-1.11 |
| **2.** | Good | 11-15 | 1.12-1.18 |
| **3.** | Fair | 16-20 | 1.19-1.25 |
| **4.** | Passable | 21-25 | 1.26-1.34 |
| **5.** | Poor | 26-31 | 1.35-1.45 |
| **6.** | Very poor | 32-37 | 1.46-1.59 |

| | | | |
|---|---|---|---|
| **7.** | Very-very poor | >38 | >1.60 |

**(i) Bulk Density:** An amount of accurately weighed powder (bulk) from each formula, antecedent jolted to interrupt any agglomerates fashioned was introduced into a 25ml measurement cylinder. Once the initial volume was discovered, the cylinder was allowed to fall into its own weight on to a tough surface from the peak of 2.5cm at 2 sec interval. The recording was continued till no additional modification in volume was noted. ((Subrahmanyam 2nd edition)

$$\textbf{Loose Bulk Density} = \frac{\textbf{Weight of powder}}{\textbf{Volume of packing}}$$

$$\textbf{Tapped Bulk Density} = \frac{\textbf{Weight of powder}}{\textbf{Tapped volume of packing}}$$

**(ii) Tapped Density:**

The measure cylinder containing an identified mass of mix was tapped for a static time. The minimum volume ($V_t$) occupied within the cylinder and therefore the weight (M) of the mixture was measured. ((Subrahmanyam 2nd edition)

$$\textbf{Tapped Density} = \frac{\textbf{Weight of mixture}}{\textbf{Minimum volume occupied}}$$

**(iii) Angle of Repose:**

A funnel was crammed to the brim and also the sample was allowed to flow effortlessly through the passage under gravity. From the cone created on a graph sheet was taken to determine the area of pile, there by evaluating the flow ability of the powder. The height of the pile and the diameter was measured. The angle of repose was determined by the formula (Subrahmanyam 2nd edition)

$$\tan\theta = \frac{h}{r}$$

**Where, θ = Angle of repose**

**h = Height**

**r = Radius**

***Angle of repose is Indicate of flow properties.**

**Table 1.5: - Relation between angles of reposes & Flow ability** (Subrahmanyam 2nd edition)

| Angle of repose | Flow ability |
|---|---|
| <25 | Excellent |

| | |
|---|---|
| 25-30 | Good |
| 30-40 | Passable |
| >40 | Very Poor |

**(iv) Uniformity of Drug Content (%Assay):**

20 tablets of various formulations will be weighed individually and powdered. The powder equivalent to average weight of tablets will weighed and drug will extracted in Methanol, the drug content will determine measuring the absorbance at 345 nm after suitable dilution using a UV/Visible Spectrophotometer .

**(v) In-Vitro Disintegration Test:**

The test carried out on 6 tablets using Phosphate buffer $P^H$ 6.8 **(Saliva $P^H$)** at 37°c ± 2°c as disintegration media and the time in second/minute was taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured. The test was performed in triplicate and mean ± SD was calculated.

**(vi) In-Vitro Drug Release Profile:**

The release rate of Montelukast from mouth dissolving tablets was determined using United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.5% SLS as a dissolution medium, at 37±2°c and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus at 2, 4, 6, 8, 10, 12, 14, 16, and 18min. The samples were filtered through a 0.45 membrane filter. Absorbance of these solutions was measured at 345 nm using a UV/VIS spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

**(vii) Release Kinetics: -**

The dissolution data was fitted to Zero order, First order, Higuchi and Korsmeyer- Peppas to ascertain the kinetic modelling of the drug release. The model was adopted for deciding the most appropriate model. Data of In-vitro release was fit into different equations to explain the release kinetics of Montelukast sodium (MDT) release from Mouth. The kinetics equation used was Zero order and First order.

**(viii) Accelerated Stability Study:**

The Orally disintegrating tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

1. 40 ± 2 °C
2. 50 ± 2 °C
3. 37 ± 2 °C and
4. Relative Humidity = 75% ± 5%

The tablets were withdrawn after a period of 15 days and analysed for physical characterization (Visual defects, Hardness, Friability, Disintegrations, and Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotting according Arrhenius equation to determine the shelf life at 25 ° C.

## EVALUATION RESULTS OF MONTELUKAST SODIUM TABLETS

### 1. Organoleptic Characteristics:-

**Table No. – 1.6:** The Organoleptic Properties of Montelukast Sodium as well as following,

| S.NO. | Organoleptic Properties | Result |
|---|---|---|
| 1. | Color | A white to pale yellow Color powder |
| 2. | Odor | Characteristics |
| 3. | Taste | Bitter |

### 2. Determination of Melting Point:

Melting point of Montelukast sodium was found to be 108.21 ±0.95°C (Table 6.1). From the observation of the melting point, the drug can be considered to be sufficiently pure for employing it is present investigation. Melting point in Merck Index is 108-110°C.

**Table No. 1.7: -** Result of Melting Point Determination of Montelukast sodium.

| Observed Melting Point (°C) | | | Mean ± S.D. (n =3) |
|---|---|---|---|
| Sample 1 | Sample 2 | Sample 3 | |
| 107.66 | 108.40 | 108.58 | 108.21 ± 0.95 |

**METHOD OF ANALYSIS RESULTS:**

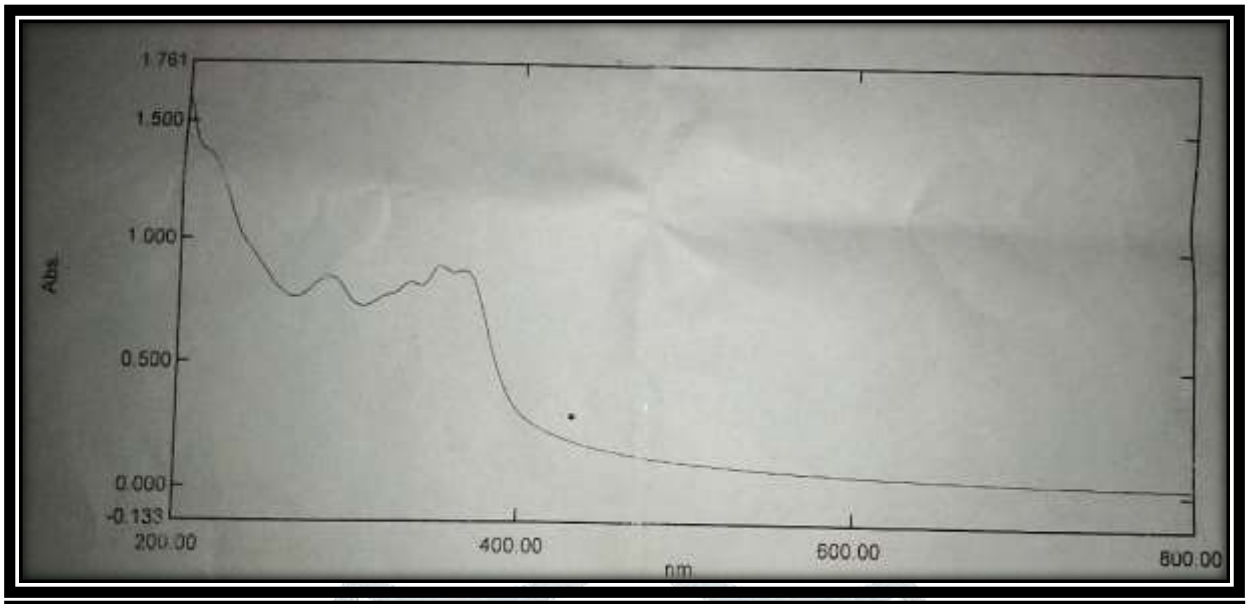
1. **Determination of Wavelength ($\lambda_{max}$) in Different Media**

The Montelukast Sodium solution (10 µg/ml) were scanned in the different media viz. distilled water, and Methanol to determine maximum absorbance in UV double beam spectrophotometer in the range from 200 nm to 400 nm. The result of UV visible spectroscopy scan of Montelukast Sodium in different medium is reported in Table.

**Table No. 1.7:** UV Absorption Maxima of Montelukast Sodium in Different Media

| S. NO | Media | λ Max (Observed) |
|---|---|---|
| **1.** | Distilled water | 353 nm |
| **2.** | Methanol | 345 nm |

**UV Absorption Maxima Curve of Montelukast Sodium in Water:-**

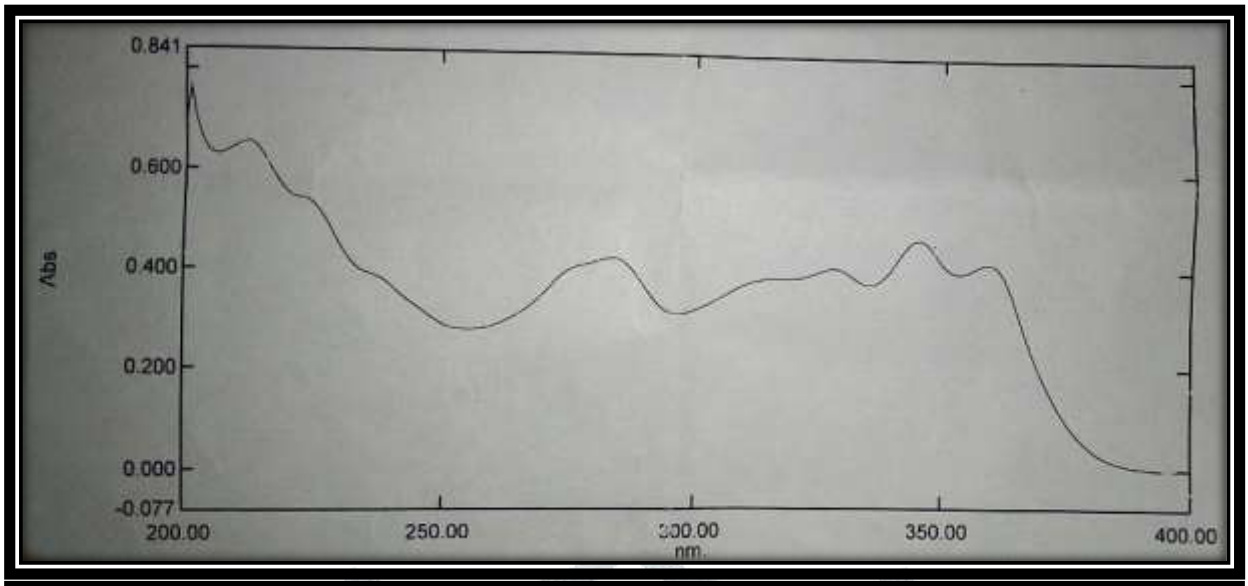



| No. | P/V | Wavelength | Abs. | Description |
|---|---|---|---|---|
| 1 | ↑ | 366.00 | 0.886 | |
| 2 | ↑ | 353.00 | 0.902 | |
| 3 | ↑ | 335.00 | 0.833 | |
| 4 | ↑ | 289.00 | 0.850 | |
| 5 | ↓ | 360.00 | 0.875 | |
| 6 | ↓ | 341.00 | 0.819 | |
| 7 | ↓ | 307.00 | 0.733 | |
| 8 | ↓ | 268.00 | 0.767 | |

**Fig.No.1.1- UV Absorption Maxima Curve of Montelukast Sodium in Water**

**Final Wavelength ($\lambda_{max}$) of montelukast Sodium is = 353 nm in Water Media**

## UV Absorption Maxima Curve of Montelukast Sodium in Methanol:-




| No. | P/V | Wavelength | Abs. | Description |
|---|---|---|---|---|
| 1 | ↑ | 359.00 | 0.416 | |
| 2 | ↑ | 345.00 | 0.465 | |
| 3 | ↑ | 328.00 | 0.406 | |
| 4 | ↑ | 283.00 | 0.426 | |
| 5 | ↑ | 212.00 | 0.656 | |
| 6 | ↓ | 353.00 | 0.395 | |
| 7 | ↓ | 335.00 | 0.373 | |
| 8 | ↓ | 296.00 | 0.314 | |
| 9 | ↓ | 255.00 | 0.281 | |
| 10 | ↓ | 206.00 | 0.630 | |

**Fig.No.1.2- UV Absorption Maxima Curve of Montelukast Sodium in Methanol**

**Final Wavelength ($\lambda_{max}$) of montelukast Sodium is = 345 nm in Methanol Media**

## 2. STANDARD PLOT OF DRUG IN DIFFERENT MEDIA:-

Standard curve of montelukast Sodium is performed in different media like,

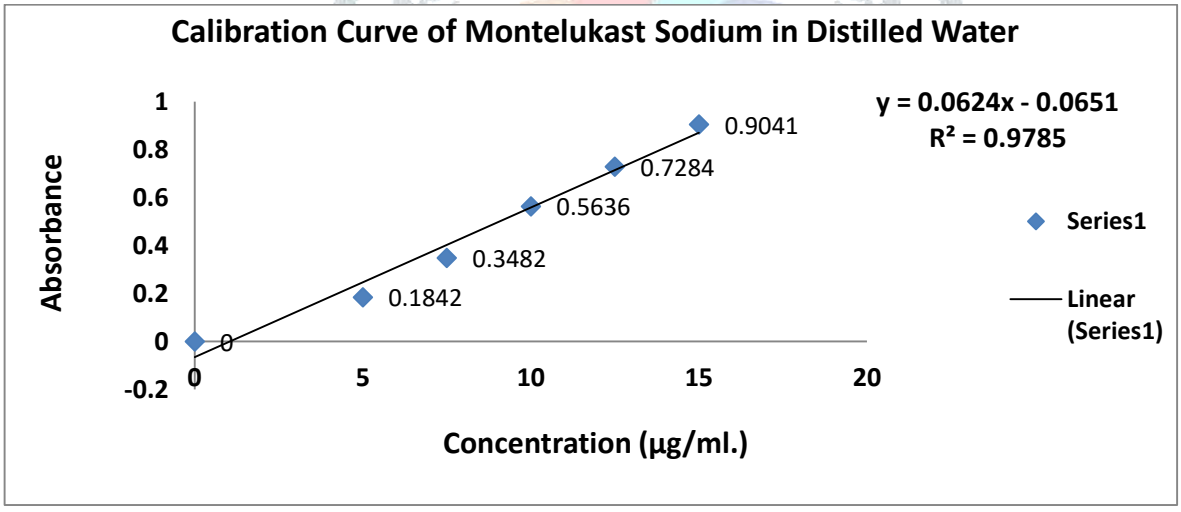
- **Distilled Water**
- **Methanol**

### 2.1 Standard Curve of Montelukast Sodium in Water ($H_2O$):-

The standard plots of montelukast Sodium were prepared in Distilled Water. The indicate that the standard curve of Montelukast Sodium in above media followed Beer law, $R^2$ values were found to be in between 0.9785 (That is in Figure) which were quite close to 1 and therefore, the linear regression equation can be used of Montelukast Sodium is Distilled Water media.

**Table No 1.8:-** Standard Plot of Montelukast Sodium in Distilled Water.

| S. No. | Concentration (µg/ml.) | Absorbance | | | Mean ± S.D. |
|---|---|---|---|---|---|
| | | Sample 1 | Sample 2 | Sample 3 | |
| **1.** | Blank | 0.0000 | 0.0000 | 0.0000 | 0.0000 ± 0.0000 |
| **2.** | 2.0 | 0.1840 | 0.1842 | 0.1844 | 0.1842 ± 0.0002 |
| **3.** | 4.0 | 0.3479 | 0.3486 | 0.3481 | 0.3482 ± 0.0003 |
| **4.** | 6.0 | 0.5632 | 0.5642 | 0.5634 | 0.5636 ± 0.0005 |
| **5.** | 8.0 | 0.7287 | 0.7280 | 0.7285 | 0.7284 ± 0.0003 |
| **6.** | 10.0 | 0.9044 | 0.9034 | 0.9045 | 0.9041 ± 0.0006 |




## 2.2. Standard Curve of Montelukast Sodium in Methanol:-

The standard plots of montelukast Sodium were prepared in Methanol. The indicate that the standard curve of Montelukast Sodium in above media followed Beer law, $R^2$ values were found to be in between 0.9996 (That is in Figure) which were quite close to 1 and therefore, the linear regression equation can be used of Montelukast Sodium is Methanol media.

**Table No.1.9:-** Standard Plot of Montelukast Sodium in Methanol.

| S. No. | Concentration (µg/ml.) | Absorbance | | | Mean ± S.D. |
|---|---|---|---|---|---|
| | | Sample 1 | Sample 2 | Sample 3 | |
| **1.** | Blank | 0.0000 | 0.0000 | 0.0000 | 0.0000 ± 0.0000 |
| **2.** | 5.0 | 0.2228 | 0.2235 | 0.2230 | 0.2231 ± 0.0003 |
| **3.** | 7.5 | 0.3387 | 0.3394 | 0.3392 | 0.3391 ± 0.0003 |
| **4.** | 10.0 | 0.4618 | 0.4627 | 0.4624 | 0.4623 ± 0.0004 |
| **5.** | 12.5 | 0.5576 | 0.5570 | 0.5579 | 0.5575 ± 0.0004 |
| **6.** | 15.0 | 0.6611 | 0.6609 | 0.6616 | 0.6612 ± 0.0003 |

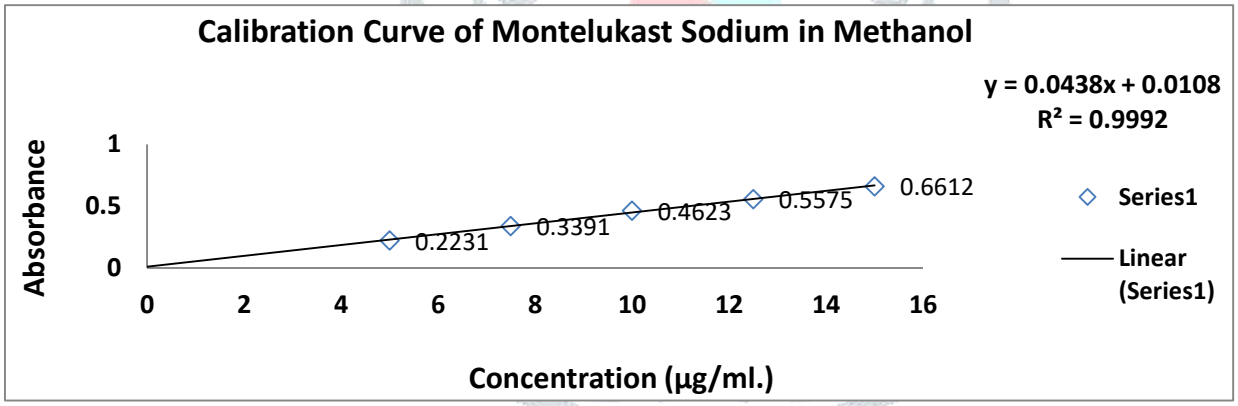



**Table No. 1.10:- Straight Line Equations and Correlation Coefficient of Drug in Different Media.**

| S. No | Media | Regression Equation | Correlation Coefficient ($R^2$) |
|---|---|---|---|
| **1** | Distilled Water | Y= 0.0624x - 0.0651 | 0.9785 |
| **2.** | Methanol | Y= 0.0438x + 0.0108 | 0.9992 |

## 3. Identification of Functional Groups by FTIR

Identification of Montelukast Sodium was carried out by the FTIR spectroscopy. The important peaks are given and depicted in Figure the characteristic peaks observed for Montelukast Sodium matched

with the reported value. Hence, the drug was identified as Montelukast Sodium and is sufficiently pure to be employed in the undertaken studies.

**Standard FTIR Spectra of Montelukast Sodium:-**

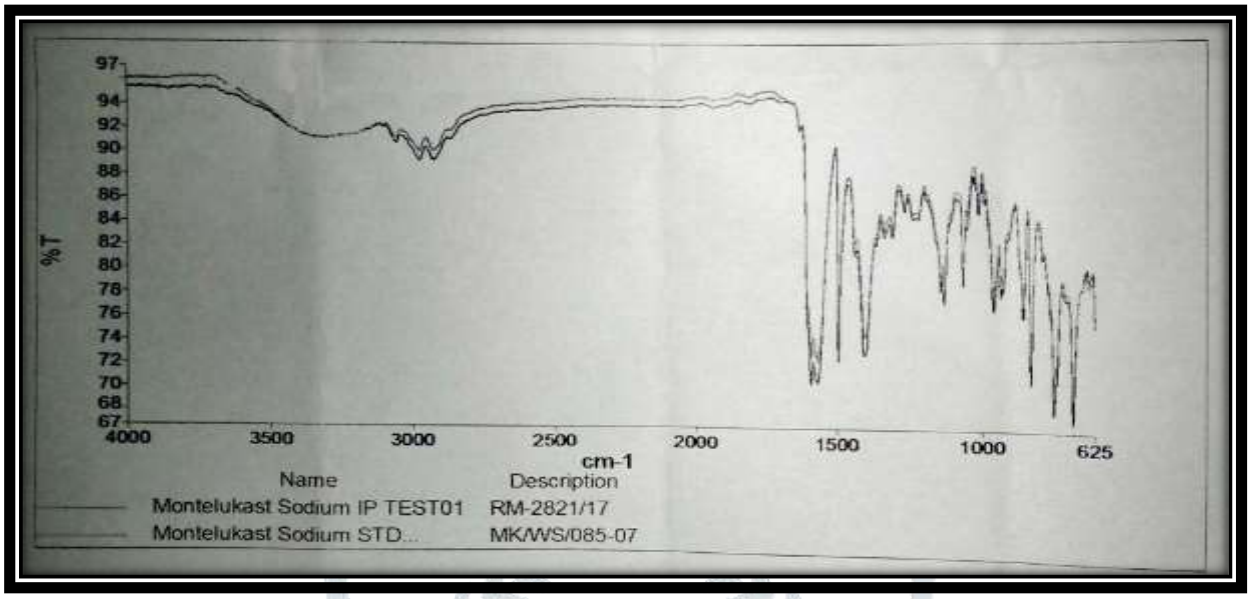



**Fig.No.1.3- Montelukast Sodium FTIR spectrum (STANDARD)**

**Sample FTIR Spectra of Montelukast Sodium: -**

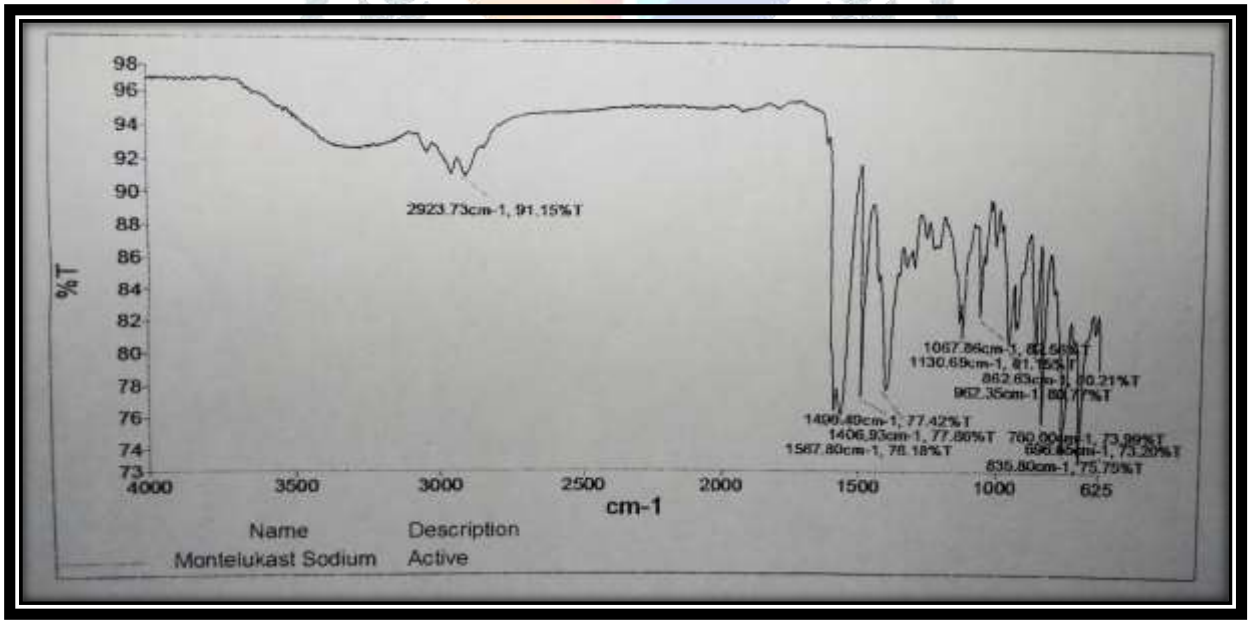



**Fig.No.1.4- Montelukast Sodium FTIR spectrum (SAMPLE)**

**FTIR Spectra of Montelukast Sodium + ALL Excipients**

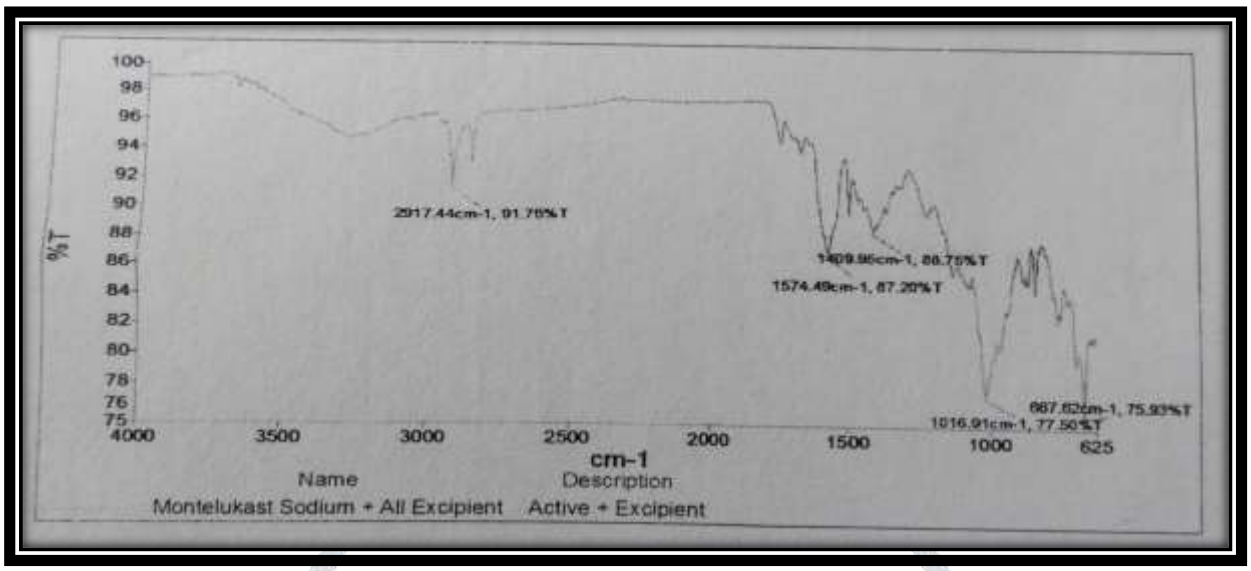



**Fig.No.1.5 - FTIR Spectra of Montelukast Sodium + All Excipients**

## 4. Solubility Profile of Drug in Distilled Water

Solubility of Montelukast Sodium in distilled water was found to be 4.98 mg/ml. The value comes under the description Slightly/Poorly soluble in water and confirm with monograph of drug.

**Table 1.11: Solubility profile of Montelukast Sodium.**

| S. No. | Solvents | Solubility (mg/ml) |
|---|---|---|
| **1** | Distilled Water | Slightly / Poorly soluble |
| **2** | Methanol | Freely soluble |
| **3** | Ethanol | Freely soluble |
| **4** | Acetonitrile (ACN) | Practically Insoluble |

## 5. Partition Coefficient (Log P) with different Solvents (Aqueous & Non-Aqueous):

Log P is the concentration of drug in organic phase (Non-Aqueous) and Aqueous Phase. The partition coefficient of Montelukast Sodium in Water was determined by using equal amount of Non-Aqueous as an oil phase and Water as the Aqueous phase. In a separating funnel these two phases were mixed in equal quantities.in solvent system required quantity of drug was mixed then the mixture was shaking by hand

shaking method until equilibrium was achieved. After that separating funnel kept aside for 20 mins after this 20 mins aqueous phase was filtered and 1 ml of this phases was taken and diluted with Water and measured the absorbance of Montelukast Sodium l in aqueous phase at 345 nm using UV-Spectrophotometer. The partition coefficient of Montelukast Sodium was calculated by using formula.

$$P_{o/w} = (C_{oil} / C_{water})\ \text{equilibrium}$$

The partition coefficient of montelukast sodium was found to be **2.33** in range. That is described the lipophilic nature of the following drug. The partition coefficient is determined by the **water & 1-octanol** (Aqueous & Non-aqueous phase). The nature of the following drug is lipophilic that means the followed formulation is good permeable by root of fast dissolving drugs, the drug is more absorbed by the root of mouth dissolving drugs.

## 6. Pre- Compression Parameter of Powder Mixture:

The pre-compression parameters are given as well as following of totally 9 formulations.

**Table.1.12: Pre- compression parameters of Montelukast sodium powders mixtures**

| S.No. | Formulation Code | Bulk Density (gm/ml) | Tapped Density (gm/ml) | Angle of Repose (tanØ) | Carr's Index (%) | Hausner's Ratio (%) |
|---|---|---|---|---|---|---|
| 1. | F-1 | 0.58 ±0.020 | 0.71±0.014 | 27°±0.60 | 18.30±3.50 | 1.22±0.050 |
| 2. | F-2 | 0.54 ±0.017 | 0.65±0.008 | 24°±0.516 | 16.92±3.23 | 1.20±0.046 |
| 3. | F-3 | 0.56±0.014 | 0.66±0.020 | 22°±0.385 | 15.15±2.42 | 1.17±0.033 |
| 4. | F-4 | 0.60±0.014 | 0.69±0.017 | 26°±0.320 | 13.04±2.06 | 1.15±0.027 |
| 5. | F-5 | 0.58±0.020 | 0.65±0.014 | 23°±0.097 | 10.76±2.53 | 1.12±0.031 |
| 6. | F-6 | 0.54±0.026 | 0.60±0.014 | 22°±0.232 | 10.0±3.77 | 1.11±0.047 |
| 7. | F-7 | 0.59±0.017 | 0.67±0.014 | 26°±0.670 | 11.94±2.25 | 1.13±0.028 |
| 8. | F-8 | 0.52±0.014 | 0.58±0.008 | 24°±0.770 | 10.34±3.16 | 1.11±0.040 |
| 9. | F-9 | 0.57±0.016 | 0.63±0.014 | 22°±0.346 | 9.52±3.36 | 1.10±0.039 |

## 7. Post- Compression Parameter of Montelukast Sodium Tablets:

The Post-compression parameters are given as well as following of totally 9 formulations.

**Table.1.13: Post- compression parameters of Montelukast sodium Tablets.**

| S.No. | Formulation Code | Weight Variation (mg) | Hardness (kg/cm$^2$) | Thickness (mm) | Friability (%) | Disintegration Time (Min/Sec.) |
|---|---|---|---|---|---|---|
| 1. | F-1 | 203.3±2.94 | 1.57±0.15 | 3.78±0.037 | 1.17±0.026 | 3.06 ± 0.25 |
| 2. | F-2 | 204.4±2.91 | 2.43±0.24 | 3.79±0.057 | 1.06±0.021 | 2.59 ± 0.23 |
| 3. | F-3 | 204.5±2.95 | 2.75±0.14 | 3.80±0.047 | 0.92±0.025 | 2.29 ± 0.047 |
| 4. | F-4 | 204.0±2.94 | 2.82±0.16 | 3.79±0.042 | 0.76±0.021 | 1.54 ± 0.036 |
| 5. | F-5 | 205.0±2.58 | 3.23±0.13 | 3.79±0.050 | 0.67±0.017 | 0.57 ± 0.014 |
| 6. | F-6 | 203.2±3.64 | 3.57±0.17 | 3.80±0.032 | 0.52±0.021 | 1.04 ± 0.017 |
| 7. | F-7 | 204.0±3.05 | 3.64±0.12 | 3.79±0.033 | 0.36±0.019 | 1.33 ± 0.076 |
| 8. | F-8 | 205.3±3.43 | 3.88±0.11 | 3.81±0.044 | 0.30±0.020 | 0.47 ± 0.34 |
| 9. | F-9 | 204.0±3.91 | 3.65±0.14 | 3.80±0.028 | 0.29±0.023 | 0.54± 0.042 |

## 8. Post- Compression Parameter of Montelukast Sodium Tablets:

The Post-compression parameters are given as well as following of totally 9 formulations.

**Table.1.14: Post- compression parameters of Montelukast sodium Tablets.**

| S.No. | Formulation Code | Water Absorption Ratio | Wetting Time (Min. / Sec.) | Drug Content (mg) | Drug Content (%) |
|---|---|---|---|---|---|
| 1. | F-1 | 64 ± 2.60 | 2.55 ± 0.033 | 4.93 ± 0.010 | 98.54 % |
| 2. | F-2 | 60 ± 2.60 | 2.42 ± 0.045 | 4.95 ± 0.020 | 99.09 % |

| | | | | | |
|---|---|---|---|---|---|
| **3.** | **F-3** | 54 ± 3.03 | 2.09 ± 0.052 | 4.91 ± 0.015 | 98.24 % |
| **4.** | **F-4** | 61 ± 3.34 | 1.37 ± 0.046 | 4.95 ± 0.026 | 98.93 % |
| **5.** | **F-5** | 50 ± 2.89 | 0.41 ± 0.039 | 4.87 ± 0.020 | 97.34 % |
| **6.** | **F-6** | 48 ± 2.16 | 0.54 ± 0.031 | 4.92 ± 0.025 | 98.35 % |
| **7.** | **F-7** | 56 ± 1.78 | 1.22 ± 0.045 | 4.96 ± 0.020 | 99.13 % |
| **8.** | **F-8** | 52 ± 2.36 | 0.44 ± 0.021 | 4.99 ± 0.010 | 99.75 % |
| **9.** | **F-9** | 45 ± 2.60 | 0.56 ± 0.022 | 4.97 ± 0.011 | 99.44 % |

**9. IN-VITRO DRUG RELEASE STUDY: -**

In-vitro dissolution was carried by dissolution apparatus type-2 release from mouth dissolving tablets prepared from drug. Montelukast sodium are shown in table, Among these formulated mouth dissolving tablets **F8** formulation was found to be best because the release of drug in 18 minutes was found to be **99.76 %.** The formulation containing Sodium starch glycolate and Croscarmellose Sodium release the drug at much faster rate in comparison to other formulations.

**Table 1.15: - % Drug release of montelukast sodium (MDT), of All formulations.**

| S.NO. | TIME (Min.) | F-1 (%) | F-2 (%) | F-3 (%) | F-4 (%) | F-5 (%) | F-6 (%) | F-7 (%) | F-8 (%) | F-9 (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| **1.** | **2.0** | 15.81 | 17.58 | 18.79 | 23.07 | 22.03 | 19.18 | 25.80 | 22.97 | 30.63 |
| **2.** | **4.0** | 29.01 | 37.87 | 32.18 | 31.55 | 34.04 | 36.57 | 40.40 | 34.46 | 43.28 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **3.** | **6.0** | 39.46 | 45.80 | 48.69 | 47.28 | 49.27 | 51.50 | 49.86 | 50.45 | 54.62 |
| **4.** | **8.0** | 44.75 | 53.69 | 61.13 | 55.25 | 62.37 | 58.20 | 62.76 | 67.93 | 66.20 |
| **5.** | **10.0** | 57.81 | 61.94 | 71.80 | 67.39 | 70.07 | 73.31 | 77.40 | 85.09 | 79.53 |
| **6.** | **12.0** | 67.55 | 68.73 | 79.28 | 72.69 | 82.59 | 87.23 | 86.07 | 93.32 | 88.02 |
| **7.** | **14.0** | 74.46 | 76.11 | 85.92 | 82.16 | 85.99 | 89.51 | 93.03 | 98.34 | 93.74 |
| **8.** | **16.0** | 82.76 | 83.70 | 91.03 | 92.43 | 90.15 | 94.52 | 98.01 | 99.48 | 98.50 |
| **9.** | **18.0** | 84.63 | 86.05 | 93.10 | 96.42 | 94.20 | 97.73 | 98.22 | 99.62 | 99.07 |

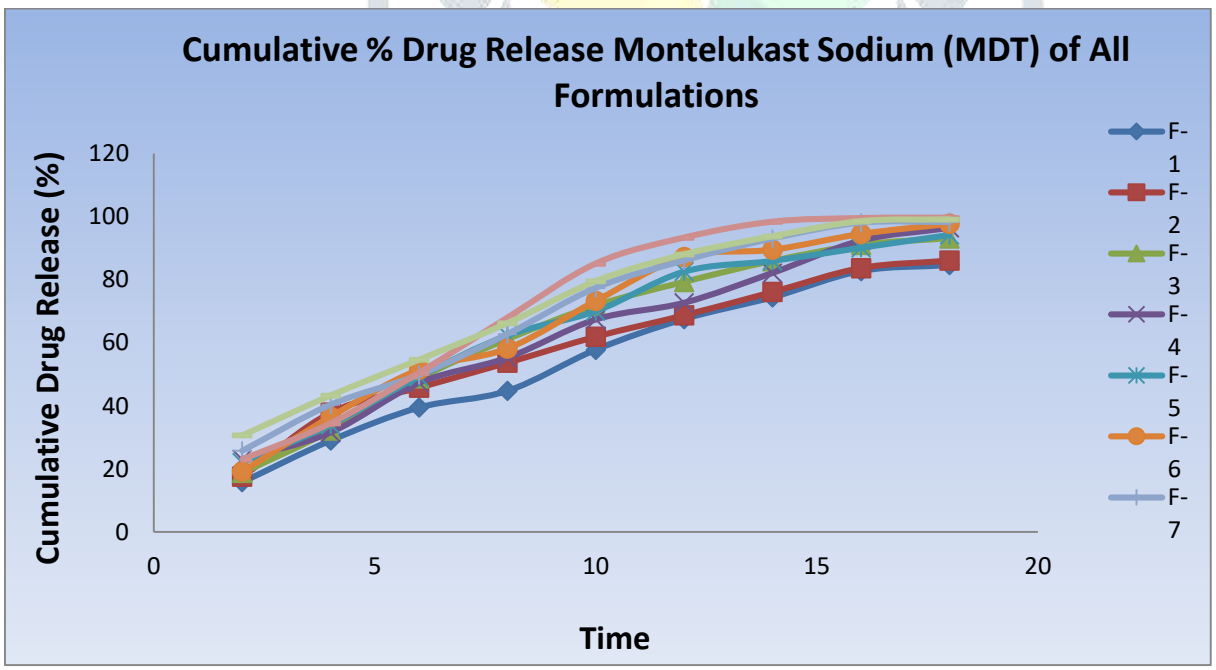



**Figure No.1.6: - Cumulative % Drug release Montelukast sodium (MDT), of All formulations.**

## 10. Release Kinetic Analysis: -

**10.1 Zero order release kinetic plot from $F_1$, $F_2$, $F_3$, $F_4$, $F_5$, $F_6$, $F_7$, $F_8$ and $F_9$ formulations of Montelukast sodium (MDT).**

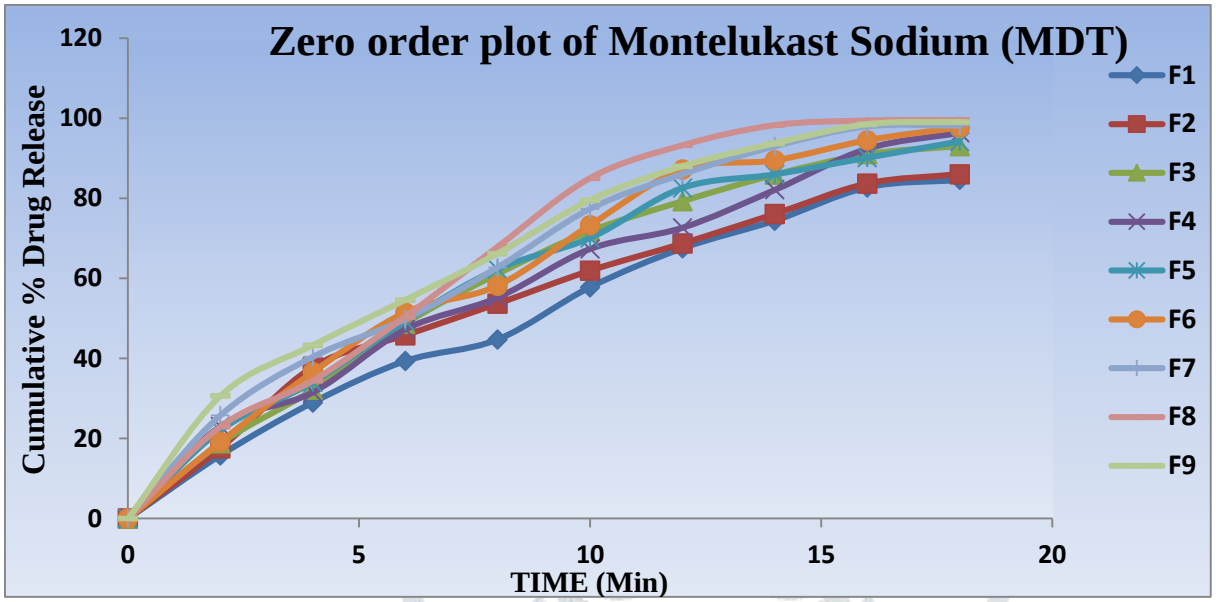



**Figure No. 1.7: - Zero order release kinetic plot from $F_1$, $F_2$, $F_3$, $F_4$, $F_5$, $F_6$, $F_7$, $F_8$ and $F_9$ formulations of Montelukast Sodium (MDT).**

**10.2 First order release kinetic plot from $F_1$, $F_2$, $F_3$, $F_4$, $F_5$, $F_6$, $F_7$, $F_8$ and $F_9$ formulations of Montelukast sodium (MDT).**

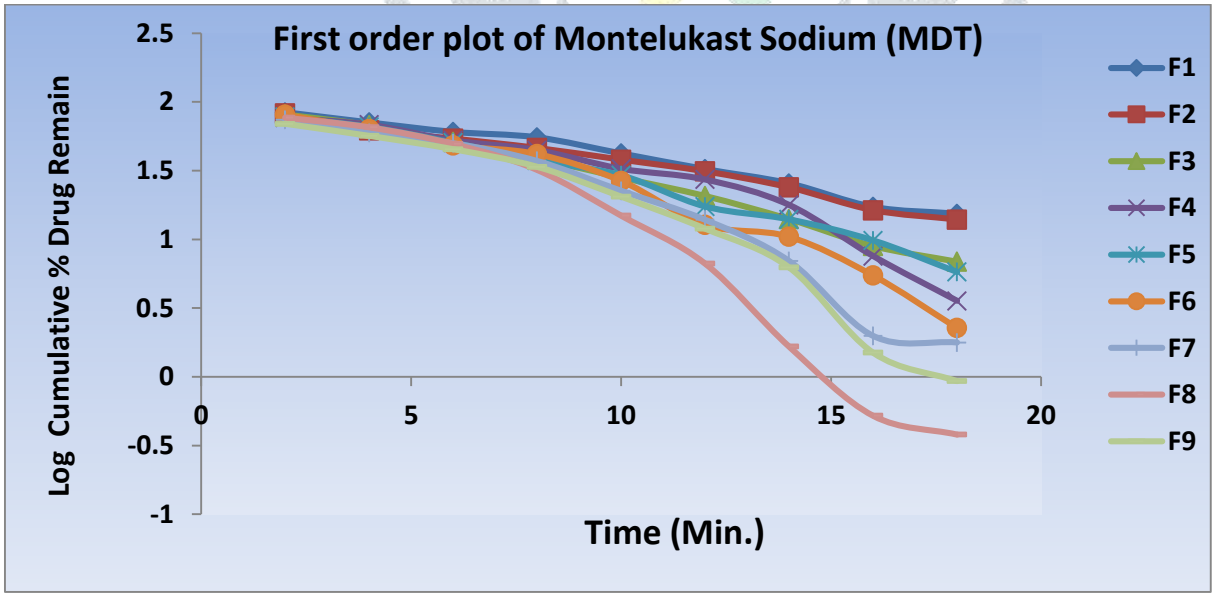



**Figure No. 1.8: - First order release kinetic plot from $F_1$, $F_2$, $F_3$, $F_4$, $F_5$, $F_6$, $F_7$, $F_8$ and $F_9$ formulations of Montelukast Sodium (MDT).**

**10.3 Higuchi release kinetic plot from $F_1$, $F_2$, $F_3$, $F_4$, $F_5$, $F_6$, $F_7$, $F_8$ and $F_9$ formulations of Montelukast sodium (MDT).**

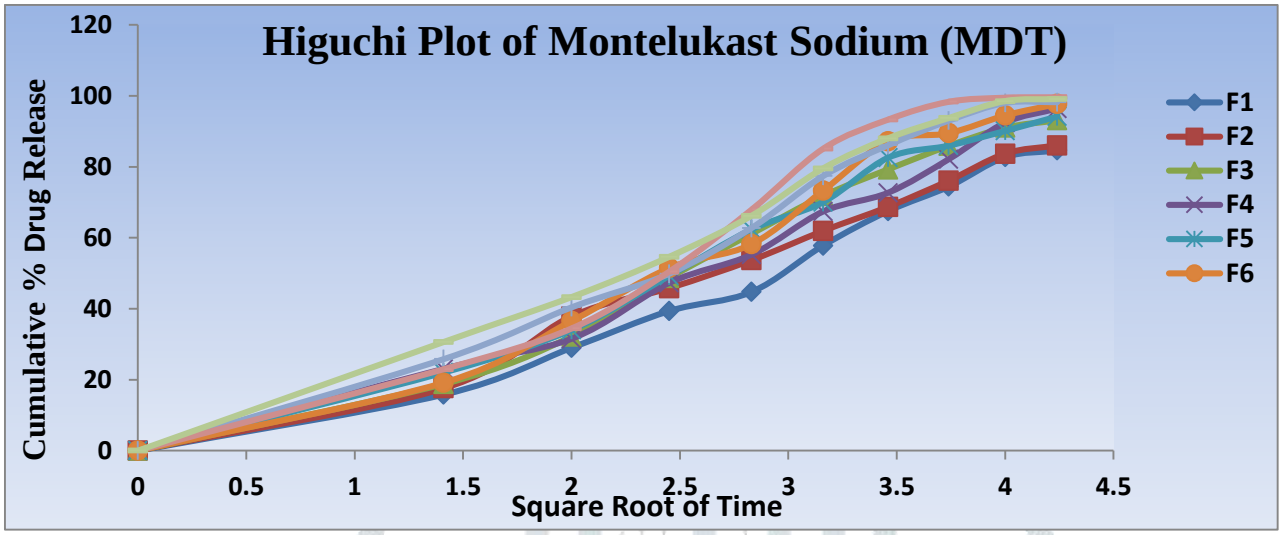



**Figure No. 1.9: - Higuchi release kinetic plot from $F_1$, $F_2$, $F_3$, $F_4$, $F_5$, $F_6$, $F_7$, $F_8$ and $F_9$ formulations of Montelukast Sodium (MDT).**

**10.4 Korsmeyer Peppas release kinetic plot from $F_1$, $F_2$, $F_3$, $F_4$, $F_5$, $F_6$, $F_7$, $F_8$ and $F_9$ formulations of Montelukast sodium (MDT).**

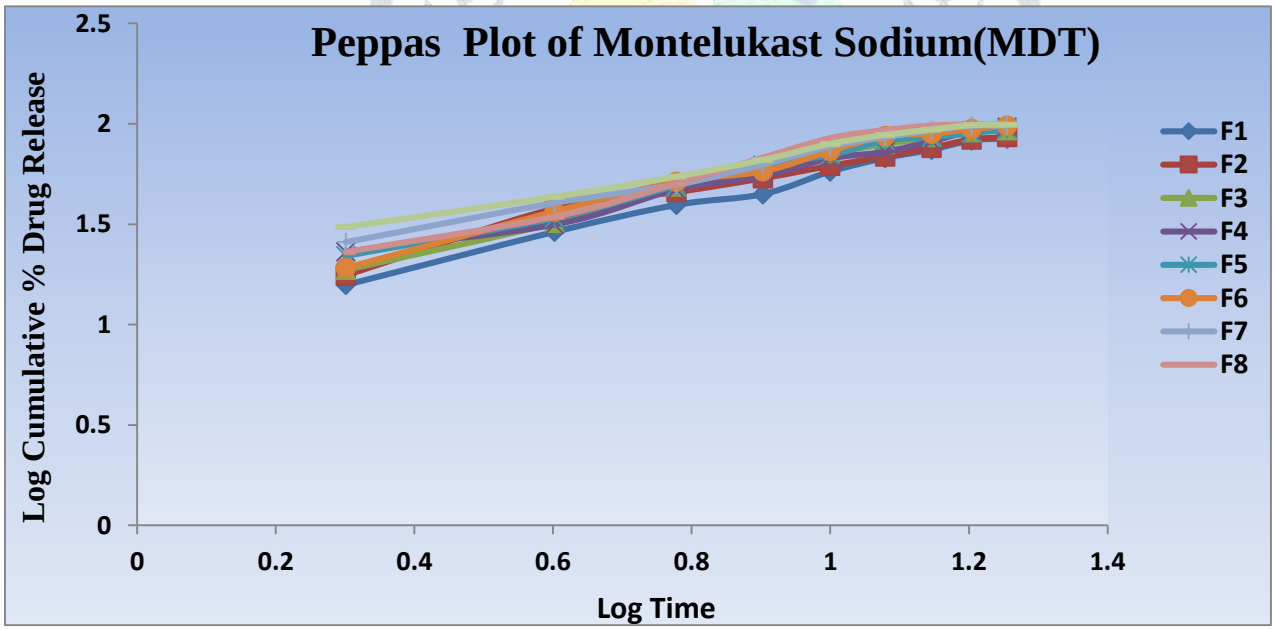



**Figure no. 1.10: - Korsmeyer Peppas release kinetic plot from $F_1$, $F_2$, $F_3$, $F_4$, $F_5$, $F_6$, $F_7$, $F_8$ and $F_9$ formulations of Montelukast Sodium (MDT).**

**11. STABILITY STUDIES:**

The Stability of a preparation is usually defined as the capacity of the formulation to remain within defined limit.

The stability studies were as per the ICH guideline by keeping for optimized mouth dissolving tablets of final formulation **(F-8)** at 40°c ± 2°c with RH 75 ± 5% for 3 month in stability chamber and tablets were with drown at every month and tested for colour, size and shape, weight variation, hardness, thickness, % friability, disintegration time, % drug content as well as result are recorded in table.

**Table-1.16: Result of stability study of optimized formulation (F-8) at 40°c ± 2°c (75 ± 5% RH)**

| Parameter | Initial | After-1-Month | After-2-Month | After-3-Month |
|---|---|---|---|---|
| **Colour** | Orange in colour | No change | No change | No change |
| **Size & Shape** | 7.5 mm in size and round in shape, both sides are plane. | No change | No change | No change |
| **Weight Variation (mg)** | 205.3±3.43 | 205.2 ±2.09 | 204.6 ± 2.59 | 204.7 ± 2.16 |
| **Thickness (mm)** | 3.81 ± 0.044 | 3.82 ± 0.034 | 3.82 ± 0.033 | 3.81 ± 0.028 |
| **Hardness ($kg/cm^2$)** | 3.8 ± 0.110 | 3.9 ± 0.166 | 3.8 ± 0.157 | 3.9 ± 0.164 |
| **% Friability** | 0.30 ± 0.020 | 0.31 ± 0.014 | 0.32 ± 0.021 | 0.30 ± 0.024 |
| **Disintegration Time (Sec.)** | 0.47 ± 0.034 | 0.49 ± 0.014 | 0.48 ± 0.017 | 0.50 ± 0.016 |
| **Drug-Content (%)** | 99.75 ± 0.01 | 99.69 ± 0.03 | 99.71 ± 0.02 | 99.65 ± 0.03 |

**IN-VITRO STUDY:-**

**Table No. 1.17: In-Vitro % Release Result of stability study of optimized formulation (F-8) at 40°c ± 2°c (75 ± 5% RH)**

| S.No. | 2.0 (Min) | 4.0 (Min) | 6.0 (Min) | 8.0 (Min) | 10.0 (Min) | 12.0 (Min) | 14.0 (Min) | 16.0 (Min) | 18.0 (Min) |
|---|---|---|---|---|---|---|---|---|---|
| **Initial Formulation % Release** | 22.97 | 34.46 | 50.45 | 67.93 | 85.09 | 93.32 | 98.34 | 99.48 | 99.62 |
| **After 3-Month % Release** | 23.41 | 35.23 | 49.90 | 68.99 | 82.66 | 92.48 | 97.01 | 98.69 | 99.15 |

**CONCLUSION: -**

The study was performed with the aim to formulation, optimization and evaluation of mouth dissolving tablets of montelukast sodium. Montelukast sodium mouth dissolving tablet final formulation was prepared by wet granulation method using croscarmellose sodium, sodium starch glycolate as superdisinteganting agent.

The release of drug from the formulation **(F-8)** was quicker when compared with other formulations. It can be included that mouth dissolving tablets prepared sodium starch glycolate (Primogel) and croscarmellose sodium have much better in-vitro dissolution as compared other formulations. The release of formulation **(F-8)** was found to be **99.62 %** in 18 minutes. The drug content of from the formulation **(F-8)** was good when compared with other with other formulations. The drug content of montelukast sodium was found to be **99.75 %** by using UV-spectroscopy method and according to the additional method for determine the drug content of final formulation of montelukast sodium by using HPLC method found to be **99.80 %** that is similar to the UV-spectroscopy method. The residual solvent study by using GC (Gas chromatography) was found to be **1816** from the limit **5000** of Iso propyl alcohol which is using in the formulations. The in vitro disintegration of from the formulation **(F-8)** was good when compared with other with other formulations. The In vitro disintegration of montelukast sodium was found to be **47** seconds.

According to the optimization of final formulation **(F-8)** is better than from the other formulations of montelukast sodium mouth dissolving tablets.

**ACKNOWLEDGEMENT: -** Mr. Pranshu Tangri and Dr. Preeti Kothiyal would like to acknowledge the support during this review article from, SGRRITS, Dehradun (U.K.) for its esteemed support and encouragement.

**REFERENCES: -**


1. Kuccherkar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets: A novel drug delivery system. Pharm Times 2003;35:3-10.
2. Martindale: The Extra Pharmacopoeia. In: Reynolds JE, editor. 31st ed.
3. Nayak SM, Gopalkumar P. Design and optimization of fast dissolving tablets for promethazine theoclate. Indian Drugs 2004;41:554-6.
4. Lachman L, Lieberman HA, Kanig JL, editors. The Theory and Practice of Industrial Pharmacy. 3rd ed. Mumbai: Varghese Publication House; 1987. p. 171-96.
5. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets of salbutamol sulphate: A novel drug delivery system. Indian Drugs 2004;41: 592-8.
6. Gohel M, Patel M, Amin A, Agrwal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. AAPS PharmSciTech 2004; 5: 1-6.
7. Abdelbary G, Prinderre P, Eouani C, Joachim J, Reynier JP, Piccerelle PG. The preparation of orally disintegrating tablets using a hydrophilic waxy binder. Int J Pharm 2004; 278: 423-33.
8. Mishra B, Panigrahi D, Baghel S. Mouth dissolving tablets: An overview of preparation techniques, evaluation and patented technologies. J Pharm Res 2005; 4:33-8.
9. Parikh SR, Gothoskar AR. Areview of mouth dissolving tablet technologies. Pharm Tech 2003; Nov [Cited 2008 Nov 9]. Available from URL: http://www.pharmtech.com.
10. Kaushik D, Dureja H, Saini TR. Mouth dissolving tablets: a review. Indian Drugs 2004; 41(4): 187-93.
11. Ganure Ashok L, Dangi Amish A, Patel Pinkal Kumar, Manish Kumar Rai, Aravadiya Jigar P. Preparation and evaluation of tramadol hydrochloride fast dispersible tablet by using compression technique. IJPI's Journal of Pharmaceutics and Cosmetology 2011; 1:2.
12. Shukla D, Chakraboty S, Singh S, Mishra B. Fabrication and evaluation of taste masked resinate of risperidone and its orally disintegrating tablet. URL available from http://dx.doi.org/10.3797/scipharm.0811-09-01;2009; 77: 309–326.
13. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. 3rd ed. Bombay: Varghese publishing house; 1986. p. 30-250.
14. Sekar V, Chellan VR, Immediate release tablets of Telmisartan using superdisintegrant- formulation, evaluation and stability studies. Chem Pharm Bull (Tokyo). 2008 April; 56(4): 575-7.
15. Subrahmanyam CVS, Thimmasetty J, Shivanand KM, Vijayendra Swamy SM. Laboratory manual of industrial pharmacy. Delhi: Vallabh Prakashan; 2006; 87-225.
16. Panigrahi D, Baghel S, Mishra B. Mouth dissolving tablets: an overview of preparation techniques, evaluation and patented technologies. J Pharm Res 2005; 4(3): 33-38
17. Dina NM, Madhu B, Shailendra KS, and Sengodan GV. Spray Dried Excipient: A novel technique for the formulation of orally disintegrating Tablets. Chem. Pharm. Bull. 2006; 54(1): 99-102.

**18.** Samita Gauri, Gaurav Kumar. Fast Dissolving Drug Delivery and its Technologies. The Pharma Innovation. 2012;1(2):34-39

**19.** Nagar Priyanka, Singh Kusum, Chauhan Iti, Verma Madhu, Yasir Mohd, Khan Azad.

**20.** Orally disintegrating tablets: formulation, preparation techniques and evaluation. Journal of Applied Pharmaceutical Science. 2011;01(04):35-45.

**21.** Panigrahi D, Baghel S and Mishra B. Mouth dissolving tablets: An overview of preparation techniques, evaluation and patented technologies. J Pharm Res 2005; 4(3):35-38

**22.** Saroha Kamal, Mathur Pooja, Verma Surender, Syan Navneet, Ajay Kumar. Mouth dissolving tablets: An overview on future compaction in oral formulation technologies. Der Pharmacia Sinica. 2010;1(1):179-187.

**23.** Mehta Kuldeep, Garala Kevin, Basu Biswajit, Bhalodia Ravi, Joshi Bhavik, Charyulu Narayana. R. An Emerging Trend In Oral Drug Delivery Technology: Rapid Disintegrating Tablets. Journal of Pharmaceutical Science and Technology. 2010; 2(10):318-329.

**24.** Chawla Gagandeep and Jain Nitin. Mouth Dissolving Tablets: An Overview. International Journal of Pharmaceutical Research & Science. 2012;3(9):2919-2925.

**25.** Debjit Bhowmik, Chiranjib B, Krishnakanth, Pankaj and Margret Chandira R. Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research, 2009; 1(1): 163-177.

**26.** Abdul Sayeed and Mohd Hamed Mohiuddin. Mouth dissolving tablets: An Overview.

**27.** International Journal of Research in Pharmaceutical and Biomedical Sciences. 2011; 2(3): 1-9.

**28.** Taksande JB, Murade SS, Trivedi RV and Umekar MJ. Formulation and Characterization of Lornoxicam Fast Dissolving Tablet Using Natural Superdisintegrants. International Journal of Research in Pharmaceutical and Biomedical Sciences. 2013; 4(2): 52-58

**29.** Mohit Mangal, Sunil Thakral, Manish Goswami and Pankaj Ghai. Superdisintegrants: A Review. International Journal of Pharmacy and Pharmaceutical Science Research. 2012; 2(2): 26-35.

**30.** Vikas Sharma and vandana aror. Comparison of various natural Superdisintegrants in the formulation of Fast Dissolving Carvedilol tablet. International Journal of Pharmaceutical Sciences and Research. 2012; 3(10): 3947-3954.

**31.** Bharat parashar, Virendra Yadav, Brajesh maury, Love Sharma. Fast dissolving tablet. International Journal of Applied Pharmaceutics. 2012; 4(2): 29-35.

**32.** Dhiraj A. Khairnar, Sanjay P. Anantwar, Chetan S. Chaudhari and Pravin A. Shelke. Superdisintegrants: an emerging paradigm in Orodispersible tablets. International Journal of Biopharmaceutics. 2014; 5(2): 119-128.

**33.** Karan Malik, Gurpreet Arora and Inderbir Singh. Ocimum Sanctum Seeds, a Natural Superdisintegrant: Formulation and Evaluation of Fast Melt Tablets of Nimesulide. Polim. Med. 2012; 42(1): 49–59.

**34.** Kaur T, Bhawandeep G, Sandeep K, Gupta GD. Mouth dissolving tablets: A novel approach to drug delivery. Int J Curr Pharm Res., **2011**, 3(1): 1-7.

**35.** Lachman L, Liberman HA and Kanig JL. Theory & practice of industrial pharmacy. 3rd ed. Mumbai: Varghese publishing house, **1991**, pp. 296-302.

**36.** C.Patil and S.Das. Effect of various superdisintegrants on the drug release profile and disintegration time of lamotrigine orally disintegrating tablets. African journal of pharmacy and pharmacology, **2011**, 5(1):76-82.

**37.** Deshika R, Viness P, Yahya EC, Lisa CT. Rapidly disintegrating oramucosal drug delivery technologies. Pharm Dev Tech., **2009**, 14(6): 588- 601

**38.** B.Venkateswara Reddy, N.Theja Vinod Kumar, K.Navaneetha. Formulation and evaluation of dispersible tablets of olmesartan medoxomil. European journal of biomedical and pharmaceutical sciences, 2015, 2(1):250-260

**39.** P.K.Lakshmi, Swetha Reddy, C. Kishore, B. Satish Reddy. Formulation and Evaluation of Oral Disintegrating Tablets of Lamotrigine Solid Dispersions. Iranian Sciences, **2013**, 9(1):1-12. Journal of Pharmaceutical Sciences, **2013**, 9(1):1-12.

**40.** Kuchekar BS, Bhise SB and Arungam V. Design of Fast Dissolving Tablets. Indian J Pharm Edu 2005; 35:150.

**41.** Shivam Singh, Ashish Masih, et al., " Fast Dissolving Tablets : A Review", International Journal of Current Pharmaceutical Research; ISSN: 0976-7066; 2017; 9(2): 8-18

**42.** Ashish Mahis, Ajay Kumar Tiwari, et al., "Formulation and Evaluation of Fast dissolving Tablets of Amoxycillin Trihydrate and Potassium Clavulanate", International Journal of Current Pharmaceutical Research; ISSN: 0975-7066; 2017; 9(2): 48-58

**43.** Sina Koosha, Mohammad Ali Shahtebi, et al., "Formulation and Evaluation of Orally Disintegrating Tablets of Ondansetron using natural Superdisintegrant", Journal of Herbmed Pharmacology;2015;4(3):102-109

**44.** Dr. B Venkateswara Reddy, K.V. Reddy, et al.," Formulation and Evaluation of Lamotrigine Mouth dissolving Tablets", International Journal of Chemistry and Pharmaceutical Sciences; ISSN:2321-3132; 2015;3(4): 1431-1435

**45.** B. Venkateswara Reddy, Vinay Kumar Reddy, et al., "Formulation and Evaluation of mouth dissolving Tablets of Mosapride Citrate", Asian Journal of Chemical and Pharmaceutical Research; ISSN: 2347-8322; 2015;3(1): 220-225

**46.** Mandeep Dahiya, Parijot Pandey, et al., " et al., " Oral disintegrating Tablets : A Review", International journal of Pharma Research & Review; ISSN: 2278-6074; 2016; 5(1): 50-62

**47.** Bookya Padmaja, Raparla Ramakrishna, et al., "Formulation and Evaluation of Fast Dissolving Tablets of Ranitidine Hcl", Journal of Pharmacy Research; ISSN: 0974-6943; 2015; 9(2): 165-169

**48.** Mayuri R Patil, Nayan A Gujarathi, et al., "Formulation and Evaluation of mouth dissolving Tablets: A Review Article", International journal of Pharmaceutical Sciences; Apr-June 2014;5(2):7-20

**49.** Viney Chawla, Kamalesh Upreti, et al. "Formulation and Evaluation of mouth dissolving film of Paracetamol", International Journal of Pharmacy and Pharmaceutical Sciences;ISSN:0975-1491,2014;6(5):200-202

**50.** Sentil Kumar B, Sumathi M, et al., " Design and Evaluation of Fast Dissolving Tablets of Mefenamic acid", International journal of Chemical and Pharmaceutical Sciences; ISSN:0976-9390; 2014;5(3):122-125

**51.** Dina M. Abd- Alaziz, Omaima A. Sammour, et al., " Efferevescent Mouth Dissolving Tablets of Domperidone : Formulation, Characterization and Pharmacokinetic Evaluation", International journal of Pharmaceutical Sciences Review and Research; 2014;24(2): 9-19

**52.** Sarita Jangra Bhyan, Bhupinder Bhyan, et al., "Formulation and Evaluation of mouth dissolving tablets containing carvidiol solid dispersion", Scholars Research Library; ISSN:0975-5071,2013;5(6):31-42

**53.** Ashish Garg, M.M. Gupta,"Mouth dissolving Tablets: A Review", Journal of drug Delivery & Therapeutics; 2013, 3(2):207-214

**54.** Erande Kumar, Joshi Bhagyashree," Mouth Dissolving tablets- A Comprehensive Review", International Journal of Pharma Research & Review; 2013,2(7):25-41

**55.** Parag Patel, Tejal Patel, et al., "Formulation and Evaluation of mouth dissolving Tablets for anti-Hypertensive Drug", Pharmagene;ISSN:2321-0974;2013;1(2):10-21

**56.** Geetika Sharma, Rupinder Kaur, et al., " Mouth Dissolving Tablets: A Current Review of Scientific Literature", International of Pharmaceutical and Medicinal Research: ISSN:2347-7008; 2013; 1(2): 73-84

**57.** Pratip Chaskar, Poonam Chaudhary, et al., "Formulation and Evaluation of Fast Disintegrating Tablets of Telmisartan", Inventi Rapid: Pharm Tech; ISSN: 0976-3783; 2013; 1(2): 1-6

**58.** Devendra Revanand Rane, Hemant Narhar Gulve, et al., "Formulation and Evaluation of Fast dissolving Tablets of Albendazole", International Current Pharmaceutical Journal; 2012;1(10):311-316