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# Formulation and Characterization of Orally Disintegrating Tablet of Mefenamic acid

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**ABSTRACT:** Today, the scientific scenario of drug delivery technology is extremely competitive and rapidly evolving with increasing demand for innovative and unique delivery system. An orally disintegrating tablet(ODT) is one such type of an innovative and unique delivery system that is rapidly gaining popularity and researchers are paying much attention to rapid dissolving technology. The Oral route is the most effective and safest route of drug administration because it allows patient to take a wide array of different drugs. The present study makes an attempt has been made to formulate orally disintegrating tablets of Mefenamic acid by direct compression and technique using various concentrations of natural super disintegrants like guar gum,gellan gum . ODT by direct compression were disintegrated 14 Sec and by wet granulation method 29 Sec. The formulated tablets were evaluated for uniformity weight,friability, thickness, weight variation, wetting time, water absorption ratio, disintegration time, and percentage of drug release.The optimized formulation F5 was compared with the marketed mefenamic acid Orally Disintegrating Tablet for the in vitro drug release profile. The results of formulation F5 was significantly superior compared to marketed mefenamic acid Orally Disintegrating Tablet.

**Keywords:** Orally disintegrating tablet, mefenamic acid, NSAIDs, direct compression, wet granulation

## I. INTRODUCTION

To Formulate drugs into an easily consumeable form is the basic requirement and need of today. The dosage form is a device used for the administration of a drug to a living being. Different type of dosage forms include tablets, syrups, suspensions, suppositories, injections, transdermal and patches having a different type of drug delivery mechanisms. A pharmacist faces a big challenge in the presence scenario when it comes to developing an ideal drug delivery system because these classical/modern dosage form have some advantages and disadvantages. In order to obtain maximum therapeutic benefit and minimum adverse effect ,the drug should be delivered to its site of action at concentration and rate that accomplishes this. physicochemical principles that governing the formulation of a drug should be studied thoroughly in order to develop a suitable dosage form [1] .As much as 50-60% of total dosage forms are administered orally. Solid dosage forms are popular because they are easy to administer, accurately dosed, self-medicating, pain-free ,as well as patient satisfaction.[2]

Tablets and capsules are the most common solid dosage forms; however, for some individuals, swallowing these dosage forms can be challenging. Drinking water is essential for oral dose forms to be swallowed.. Whenever water is not unavailable, in the case of motion sickness (kinetosis), and unexpected episodes of coughing during the common cold, allergic condition, and bronchitis, people frequently experience difficulty swallowing conventional dosage forms such as tablet.As a result, tablets that dissolve or disintegrate quickly in the oral cavity have attracted much interest..[3] 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. [1]

### Orally disintegrating tablet

A novel drug delivery system known as Orodispersible tablets (Orally disintegrating tablet) has been developed. Orally disintegrating tablets are superdisintegrant-based solid unit dosage forms. which will assist them in dissolving the tablet in the mouth in the availability of saliva in under a minute without difficulty swallowing. Bioavailability is significantly higher in these cases than it is with typical tablet dosage. [4]

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United States Food and Drug Administration (USFDA) defined orally disintegrating tablet as "a solid dosage form containing a medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue" they are also known as mouth dissolving tablets, melt-in mouth tablets, fast dissolving tablets, rapid melts, porous tablets and quick dissolving tablets.[5]

Mefenamic acid is a member of the anthranilic acid derivatives,chemically it is a N-(2,3-xylyl)-2-aminobenzoic acid or N-2,3-xylylanthranilic acid. is a member of the fenamate group of nonsteroidal anti-inflammatory drugs (NSAIDs) agent with analgesic, anti-inflammatory, and antipyretic properties. Mefenamic acid binds the prostaglandin synthetase receptors COX-1 and COX-2, inhibiting the action of prostaglandin synthetase. As these receptors have a role as a major mediator ofinflammation and/or a role for prostanoid signaling in activity-dependent plasticity, the symptoms of pain are temporarily reduced. It is formulated to treat rheumatoid arthritis, osteoarthritis, dysmenorrhea, and mild to moderate pain, inflammation, and fever.Mefenamic acid is rapidly absorbed after oral administration.[6]

The present study isto formulate and characterize of orally disintegrating tablet (ODT) of Mefenamic acid Natural superdisintegrents like guar gum and gellan gum.along withto mask the bitter taste of drug thus serving as a better alternative to dispersible marketed tablet.to An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.and quick onset of action is produced by rapid dissolution and absorption of the drug. Also Comparative study between optimized trial formulation and dispersible marketed formulation.as well as comparison between two conventional methods of tablet compression.

## II. MATERIALS AND METHODS

Mefenamic acid was obtained as a gift sample from HealthGenic Chemicals PVT.Ltd.Mumbai.Guar gum,gellan gum purchased from sisco research lab pvt.ltd, sodium bicarbonate,tartaric acid, purchased frommolychem (Mumbai) ,mannitol,microcrystalline cellulose(Avicel PH 102),corn starch purchased fromS.D fine chemical (Mumbai),talc ,magnesium stearate purchased from molychem (Mumbai). Milk powder purchased of nestle@brand,Aspartem purchased from molychem (Mumbai).
All other chemicals used were of analytical grade.

**Preformulation studies**
**Authentication of drug**

The drug was authenticated by, melting point determination (capillary tube method) on a Thiele's tube, differential scanning calorimeter (HITACHI),and Fourier-transform infrared spectroscopy (SHIMADZU) FTIR spectrum of drug was shown in Fig. 1 and DSC thermograph was shown in Fig. 2

**Construction of calibration curve by UV spectrophotometer**

100mg of drug was accurately weighted and transferred into a 100 ml volumetric flask containing 40 ml of methanol .this solution was sonicated for 20 min and volume was made up to 100 ml with 6.8 PH phosphate buffer to get a concentration of 1000 ug/ml of solution. From this solution, 10ml was pipetted out in 100 ml volumetric flask and diluted to 100 ml with 6.8 PH phosphate buffer to get a stock solution of 100ug /ml. from this stock solution, standard drug solution 4,8,12,16,20 and 24ug/ml concentration were prepared. Absorbance of each solution was measured at λ 279 nm against 6.8 PH phosphate buffer as blank in UV spectrophotometer and caliberation curve was constructed**.**

**Drug-excipients compatibility studies**

The goal of this research was to determined if the various proposed excipients could be used in drug formulation. For one month, open and closed vials containing binary mixtures in specific ratios were placed at 40 °C / 75 % RH and 25 °C / 60 % RH. After the stability testing was completed, any changes in the physical appearance of the sample were evaluated.

**Formulation process**
**Procedure of direct compression method**

Mefenamic acid oral dispersible tablets were made using the direct compression technique and the formula shown in table 1. The dispensed drug and all excipients were individually sifted through a 40# sieve. Weigh the drug and all of the ingredients precisely. Before weighing, sodium bicarbonate and tartaric acid were heated for 10-15 minutes at 80°C. By spatulation, the drug and all ingredients are combined, and then sodium bicarbonate and tartaric acid are added. The tablet

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mixture was then compressed (8 mm diameter, flate punch) on a rotary tablet compression machine with 8 stations (karnavati).

| Ingredients | F1 mg | F2 mg | F3 mg | F4 mg | F5 mg | F6 mg | F7 mg | F8 mg | F9 mg | F10 mg |
|---|---|---|---|---|---|---|---|---|---|---|
| **Mefenamic acid** | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| **Guar gum** | 5 | - | 10 | - | 15 | - | 20 | - | 25 | - |
| **Gellan gum** | - | 5 | - | 10 | - | 15 | - | 20 | - | 25 |
| **Sodium bicarbonate** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Tartaric acid** | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| **Mannitol** | 37 | 37 | 70 | 70 | 27 | 27 | 60 | 60 | 17 | 17 |
| **Microcrystalline cellulose** | 65 | 65 | 27 | 27 | 65 | 65 | 27 | 27 | 65 | 65 |
| **Milk powder** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Talc** | 5 | **5** | 5 | **5** | 5 | 5 | 5 | **5** | 5 | **5** |
| **Magnesium stearate** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Aspartame** | **5** | 5 | **5** | 5 | 5 | 5 | **5** | 5 | **5** | 5 |

**Table no 1 : Formulation table of trial batches ( F1-F10) by Direct compression method**

**Procedure of wet granulation method**

Mefenamic acid oral dispersible tablets were made using the wet granulation technique and the formula shown in table 2. the drug dispensed and all excipients separately In a mortar, combine the drug and mannitol, then add the required amount of 5 percent corn starch paste and prepare the dough. The wet mass was then passed through an 18# sieve, and the granules retained on a 40# sieve were collected and dried in an oven.weigh the granules and fines collected below 40#(10% wt. of granules).Calculate the amount of extragranules and other ingredients needed, then blend all of the granules. The tablet mixture then was compressed (8 mm diameter, flate punch) on a rotary tablet compression machine with 8 stations (karnavati).

| Ingredients | F11 mg | F12 mg | F13 mg | F14 mg | F15 mg | F16 mg | F17 mg | F18 mg | F19 mg | F20 mg |
|---|---|---|---|---|---|---|---|---|---|---|
| **Mefenamic acid** | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| **Guar gum** | 5 | - | 10 | - | 15 | - | 20 | - | 25 | - |
| **Gellan gum** | - | 5 | - | 10 | - | 15 | - | 20 | - | 25 |
| **Sodium bicarbonate** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Tartaric acid** | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| **Mannitol** | 102 | 102 | 97 | 97 | 92 | 92 | 87 | 87 | 82 | 82 |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Milk powder** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Talc** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Magnesium stearate** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Aspartame** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Maize starch paste (5%)** | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S | Q.S |

**Table no 2: Formulation table of trial batches (F11-F20) by Wet granulation method**

**Evaluation**

**Pre-compression parameters**

**Bulk density [7]**

It is defined as the weight of a large number of material particles divided by the volume they occupy. Particle volume, inter-particle void volume, and internal pore volume are all included in the total volume. It is the ratio of powder bulk mass to powder bulk volume. It is represented by the letter pb.Bulk density is used to find out homogeneity.

Bulk density (ρb) = M/Vb

Where M is the mass of the sample,

Vb bulk volume.

**Tapped density[8]**

It is the weight of the powder divided by the minimum volume of the measuring cylinder. A graduated cylinder containing a known weight of drug or formulation is placed on a mechanical tapper apparatus, which is operated at a fixed number of taps (50) until the powder bed reaches a minimum volume. [1, 9, 10].

Tapped density (ρt) = weight of powder blend/Minimum volume occupied by cylinder

**Hausner ratio[9]**

The Hausner ratio is an indirect measure of the ease with which powder flows. The following formula is used to calculate it.

Hausner ratio = tapped density / bulk density

Lower hausner ratio (<1.25) indicate better flow properties than higher ones (>1.25).

**Carr's compressibility index [10]**

The simplex method of measuring the free flow of powder is compressibility, which gives an indication of how easily a material can be induced to flow. The compressibility index of the granules has been determined by Carr's compressibility index (C), which is determined using the following formula.

$C = [(\rho t - \rho b/\rho t)] \times 100$

**Angle of repose [11]**

The fixed funnel method was used to calculate the angle of repose. The mixture was poured through a funnel that could be raised vertically to achieve the maximum cone height (h). Using a formula, the radius of the heap (r) was evaluated and the angle of repose was calculated. [1, 6, 7].

$\theta = \tan^{-1}(h/r)$

Where θ is the angle of repose,

h is the height of pile and r is the radius of the base pile.

**Post compression parameters**

**Uniformity of weight [12]**

The average weight of 20 tablets was determined after they were chosen at random. Individual tablets were then weighed. The I.P. weight variation specification is shown below.

| Average weight of tablet | % deviation |
|---|---|
| 80mg or less | ±10 |
| More than 80 mg but less than 250 mg | ±7.5 |
| 250mg or more | ±5 |

**Table No 3: Limits of the weight variation of Tablets:**

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**Thickness [13]**
Each batch's tablets were chosen and measured for thickness using digital vernier callipers. A micrometer was used to measure the thickness of ten tablets.

**Hardness of the tablets [14]**
During handling and transportation, the tablet should be resistant to mechanical stress. Monsanto hardness tester was used to test the hardness.. And expressed in $kg/cm^2$.

**Friability of tablets [15]**
The preweighted tablet was placed in the Roche friabilator and run for 100 revolutions at 25 rpm for 4 minutes. The tablets were cleaned and reweighted; the loss in tablet weight is the measure of friability, which is expressed as a percentage.
Percent friability = initial weight- final weight/initial weight x 100

**Wetting Time [16]**
A piece of tissue paper folded twice was placed in a perti dish (d=6.5cm) containing approximately 6ml of eosin dye. A tablet was placed on the paper, and the time it took for the orange colour to develop on the upper surface of the ODT was recorded.

**Water absorption ratio [17]**
To calculate the water absorption ratio, the weight of the ODT before placing it in the petri dish was recorded (Wb). The wetted tablet was removed from the petri dish and reweighed (Wa). The water absorption ratio (R) can be calculated using the following equation.
$R= (Wa-Wb)/Wb \times 100$
Where R= water absorption ratio, Wa= weight of the tablet after absorption, Wb = weight of the tablet before absorption.

**Disintegration test [18]**
The tablet disintegration test apparatus was used to determine the disintegration time for all formulations. Six tablets were separately placed in each tube of the disintegration test apparatus. The water was kept at 37 °± 0.5 °C, and the time it took for the whole tablet to disintegrate totally was recorded.

**Content uniformity**
Twenty tablets were powdered, and powder equivalent to 100 mg of mefenamic acid was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 40 ml methanol was added and sonicate for 20 min. Then, the volume was made up to 100 ml with phosphate buffer PH 6.8. The solution was filtered, diluted suitably with phosphate buffer PH 6.8 and analyzed spectrophotometrically at 279 nm.

**In vitro drug release studies**
In vitro drug release studies were carried out by using USP XXIII Dissolution Apparatus II (Paddle Type) at 50 rpm. The drug release profile was studied in 900 ml of phosphate buffer solution, pH 6.8 maintained at 37 ± 0.5°C. Aliquots of 5 ml of dissolution medium were withdrawn at specific time intervals (5, 10, 15,20,30,45 and 60 min.) and each time the volume withdrawn was replenished with fresh solvent. The collected samples were analyzed at 279 nm using dissolution medium as blank. The cumulative percentage drug release was calculated.

**Stability studies**
The selected formulation F5 was tested for its stability studies. Optimize formulation(F5) of orally disintegration tablet of drug were packed in HDPE container and placed container in secondary packaging which was a transparent polythene bag .the packed formulation were stored in a stability chamber under three condition i.e. room temperature ,25℃ ±2℃/ 60% RH , and 40℃ ± 2℃ / 75% RH for a period of one month and three month . After every month tablet were evaluated for appearance, hardness, uniformity of weight, drug content, in vitro disintegration time, wetting time, in vitro dissolution studies.

## III. RESULTS AND DISCUSSION

**Authentication of drug**

**1. Melting point determination of drug**
The melting point of Mefenamic Acid by capillary method was found to be approximately 231℃ , according to literature survey is 230 - 232℃.It gave authentication of pure drug

**2. Fourier transform infrared ( FTIR) spectroscopy of drug:**
The FTIR graph was derived for the identification of the various functional groups. The FTIR spectra of mefenamic acid consisted of many sharp peaks that confirm the microcrystalline nature of the drug. The observed FTIR peaks of mefenamic acid were matching with the reported peaks, as shown in Table No 4

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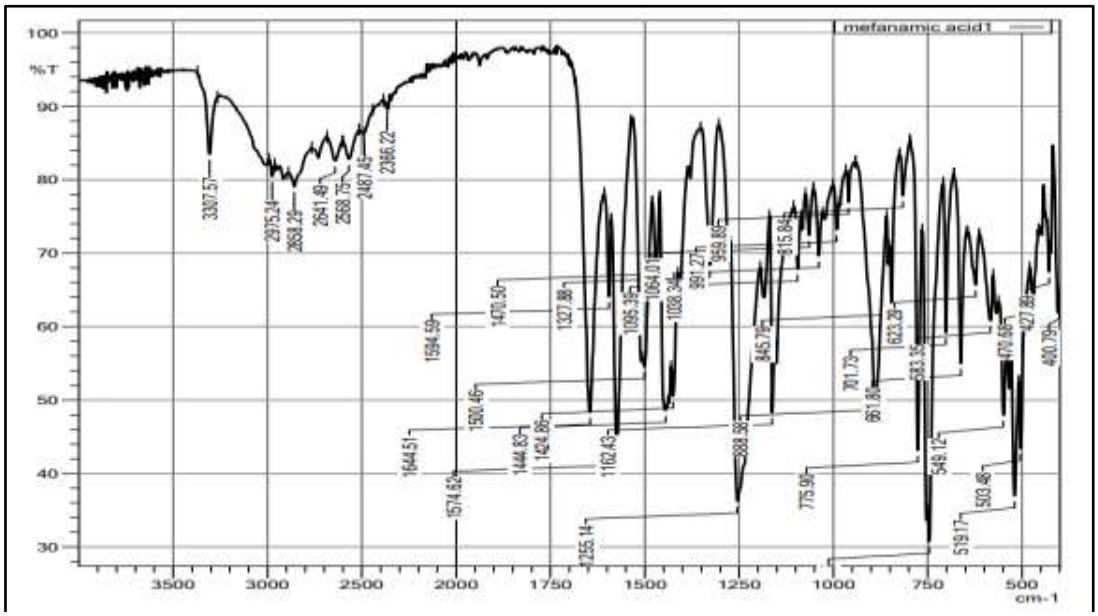


**Fig No 1: Fourier transform infrared (FTIR) spectrum of mefenamic acid**

| Functional group | Observed frequency ($cm^{-1}$) |
|---|---|
| C-H | 2858.29 |
| N-H | 3307.57 |
| $C_6H_6$ | 1574.62 |
| O-H of COOH | 2858.29 |
| C=O of COOH | 1644.51 |

**Table No 4:Functional group and observed frequency of mefenamic acid by FTIR spectroscopy**

**Differential scanning calorimetry**

**DSC of Pure drug**

DSC analysis was performed to evaluate the thermal behavior of mefenamic acid. The mefenamic acid showsa sharp endothermic peak due to the melting of a drug at 232°C corresponding reported to the melting point of the pure drug at 232°C. The sharp endothermic peak shows the semi crystalline nature of the drug. DSC of the pure drug is shown in Fig No 2

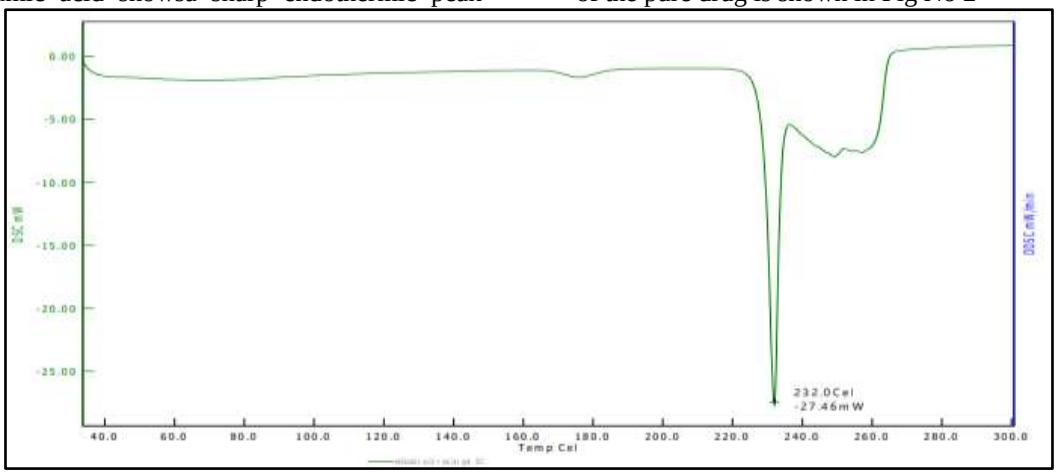


**Fig No 2: DSC Thermogram of mefenamic acid**

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**DSC of mefenamic acid with guar gum**

DSC thermogram of mefenamic acid with guar gum are shown in Fig No 3. the fig showed the characteristics of melting endotherm of mixture confirming semicrystalline nature with the no interaction between the mix.

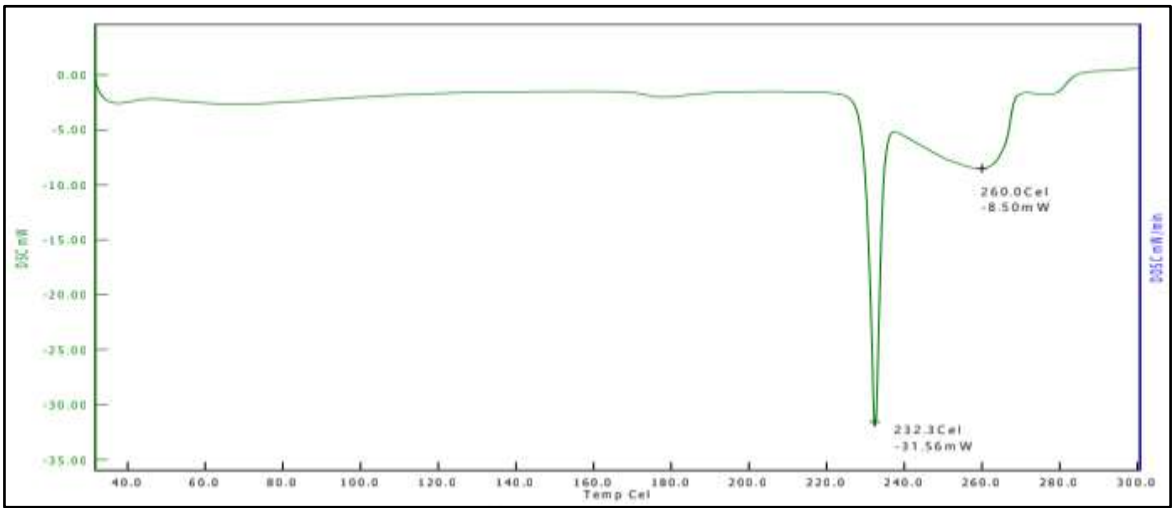


**Fig No 3: DSC Thermogram of mefenamic acid with guar gum**

**DSC of mefenamic acid with gellan gum**

DSC thermogram of mefenamic acid with gellan gum are shown in Fig No 4. the fig showed the characteristics of melting endotherm of mixture confirming semicrystalline nature with the no interaction between the mix.

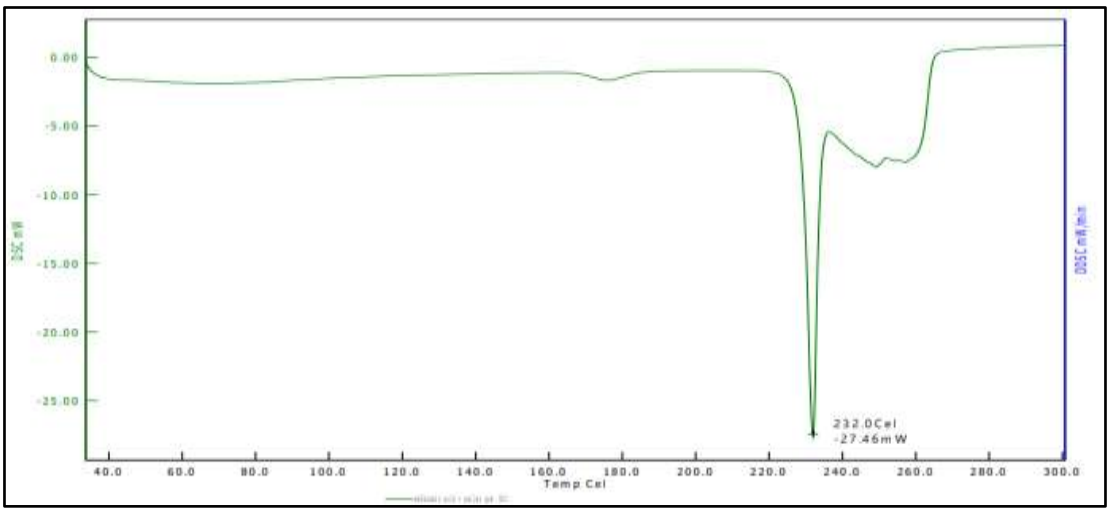


**Fig No 4: DSC Thermogram of mefenamic acid with gellan gum**

**PH solubility studies of drug**

Solubility of the drug was determined in 4 different media, given in Table No 5. According to the results, it can be concluded that the mefenamic acid provides highest solubility in phosphate buffer with PH 6.8 ,medium solubility in phosphate buffer with PH 7.4 and 0.1 N HCL and lowest solubility in Distilled water.

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| Sr. no | Media | Solubility (mg/ml) |
|---|---|---|
| 1 | Distilled water | 0.0847 |
| 2 | 0.1 N HCL | 0.2432 |
| 3 | PH 6.8 | 0.3401 |
| 4 | PH 7.4 | 0.3240 |

**Table No 5: PH solubility studies of Mefenamic acid**

**Calibration curve of mefenamic acid**

The calibration curve was determined by UV–spectrometer. Calibration curve prepared in a combination of methanol and phosphate buffer PH 6.8 at 279nm. The data had a correlation coefficient of 0.9999, slope 0.0391, and Y-intercept 0.0275. These results indicate that there is a linear relationship between concentration (4–24 µg/ml) and absorbance, as mention in Fig No 6

| Concentration (ug/ml) | Absorbance at 279 nm |
|---|---|
| 4 | 0.18 |
| 8 | 0.341 |
| 12 | 0.501 |
| 16 | 0.652 |
| 20 | 0.808 |
| 24 | 0.963 |

**Table No 6: Concentration ranges between 4 -24 ug/ml with absorbance**

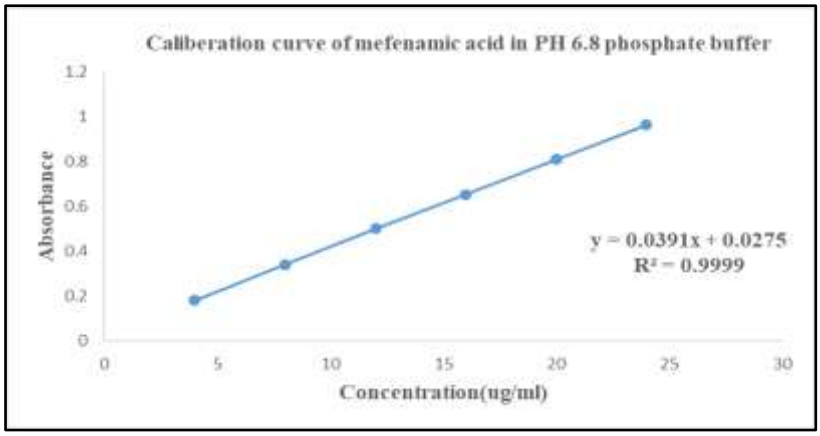


**Fig No.5: Calibration curve of mefenamic acid byUV spectrophotometry in PH 6.8 phosphate buffer**

**Screening of polymers**

Polymer screening was done according to swelling index and release behavior of various polymer using various concentration.Highest swelling property was observed in guar gum and gellan gum and moderate swelling property observed in xanthum gum and lowest in sodium alginate shown in Table No 7

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| Natural polymer | Swelling index (%) |
|---|---|
| Guar gum | 90.43±0.39 |
| Gellan gum | 84.32±0.76 |
| Xanthum gum | 80.89±1.23 |
| Sodium alginate | 72.56±0.85 |

**Table No7:Screening of polymer**

**1. Precompression evaluation parameter of tablet**

| Batches | Bulk density g/cm$^3$ | Tapped density g/cm$^3$ | Hausners ratio | Carr's index % | Angle of repose θ |
|---|---|---|---|---|---|
| **F1** | 0.509 ± 0.02 | 0.559 ± 0.06 | 1.09 ± 0.03 | 8.94 ± 0.11 | 28.04 ± 0.16 |
| **F2** | 0.502 ± 0.01 | 0.555 ± 0.01 | 1.10 ± 0.01 | 9.54 ± 0.05 | 30.45 ± 0.05 |
| **F3** | 0.503 ± 0.01 | 0.554 ± 0.02 | 1.10 ± 0.01 | 9.20 ± 0.04 | 25.31 ± 0.19 |
| **F3** | 0.504 ± 0.01 | 0.553 ± 0.03 | 1.09 ± 0.01 | 8.86 ± 0.14 | 27.87 ± 0.05 |
| **F4** | 0.503 ± 0.01 | 0.555 ± 0.02 | 1.10 ± 0.02 | 9.36 ± 0.06 | 29.56 ± 0.04 |
| **F5** | 0.502 ± 0.02 | 0.556 ± 0.02 | 1.10 ± 0.01 | 9.71 ± 0.03 | 27.25 ± 0.02 |
| **F6** | 0.506 ± 0.01 | 0.555 ± 0.03 | 1.09 ± 0.02 | 8.82 ± 0.05 | 26.23 ± 0.06 |
| **F7** | 0.505 ± 0.02 | 0.557 ± 0.01 | 1.10 ± 0.02 | 9.33 ± 0.09 | 29.67 ± 0.11 |
| **F8** | 0.506 ± 0.01 | 0.553 ± 0.02 | 1.09 ± 0.01 | 8.49 ± 0.10 | 27.98 ± 0.21 |
| **F9** | 0.505 ± 0.02 | 0.555 ± 0.03 | 1.09 ± 0.02 | 9.90 ± 0.08 | 28.87 ± 0.19 |
| **F10** | 0.507 ± 0.02 | 0.554 ± 0.02 | 1.09 ± 0.01 | 8.48 ± 0.04 | 26.65 ± 0.16 |
| **F11** | 0.595 ± 0.06 | 0.622 ± 0.03 | 1.04 ± 0.01 | 4.34 ± 0.11 | 29.76 ± 0.15 |
| **F12** | 0.597 ± 0.04 | 0.626 ± 0.03 | 1.04 ± 0.02 | 4.63 ± 0.15 | 29.50 ± 0.18 |
| **F13** | 0.594 ± 0.05 | 0.625 ± 0.02 | 1.05 ± 0.01 | 4.96 ± 0.13 | 26.87 ± 0.05 |
| **F14** | 0.598 ± 0.04 | 0.633 ± 0.15 | 1.05 ± 0.01 | 5.52 ± 0.06 | 27.54 ± 0.09 |
| **F15** | 0.596 ± 0.05 | 0.638 ± 0.09 | 1.07 ± 0.02 | 6.58 ± 0.03 | 28.67 ± 0.06 |
| **F16** | 0.601 ± 0.03 | 0.639 ± 0.10 | 1.06 ± 0.02 | 5.94 ± 0.08 | 28.89 ± 0.10 |
| **F17** | 0.600 ± 0.02 | 0.641 ± 0.10 | 1.06 ± 0.01 | 6.39 ± 0.11 | 26.87 ± 0.03 |
| **F18** | 0.602 ± 0.01 | 0.643 ± 0.08 | 1.06 ± 0.02 | 6.37 ± 0.18 | 29.90 ± 0.02 |
| **F19** | 0.603 ± 0.02 | 0.644 ± 0.07 | 1.06 ± 0.01 | 6.36 ± 0.16 | 30.65 ± 0.04 |
| **F20** | 0.603 ± 0.01 | 0.646 ± 0.07 | 1.07 ± 0.02 | 6.65 ± 0.24 | 29.78 ± 0.05 |

Note: All values are expressed as mean±SD. n=3.

**Table No 8: Precompression evaluation parameter for orally disintegrating tablet of Mefenamic acid**

**2. Post compression evaluation parameter of tablet:**

| Batch | Uniformity of weight(mg) | Thickness (mm) | Hardness ( kg/cm$^2$) | Friability (%) |
|---|---|---|---|---|
| **F1** | 250 ± 0.38 | 5.2 ± 0.12 | 3.3 ± 0.02 | 0.07 ± 0.13 |
| **F2** | 252 ± 0.23 | 5.1 ± 0.18 | 3.4 ± 0.13 | 0.10 ± 0.03 |
| **F3** | 251 ± 0.46 | 5.1 ± 0.21 | 2.3 ± 0.24 | 0.48 ± 0.23 |
| **F4** | 249 ± 0.32 | 5.2 ± 0.17 | 2.6 ± 0.09 | 0.43 ± 0.04 |
| **F5** | 250 ± 0.20 | 5.1 ± 0.02 | 3.2 ± 0.02 | 0.08 ± 0.03 |
| **F6** | 251 ± 0.35 | 5.1 ± 0.04 | 2.3 ± 0.05 | 0.54 ± 0.24 |
| **F7** | 248 ± 0.34 | 5.2 ± 0.13 | 2.7 ± 0.23 | 0.43 ± 0.16 |
| **F8** | 250 ± 0.26 | 5.0 ± 0.04 | 2.3 ± 0.31 | 0.56 ± 0.17 |
| **F9** | 252 ± 0.34 | 5.2 ± 0.12 | 3.8 ± 0.23 | 0.09 ± 0.24 |

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| | | | | |
|---|---|---|---|---|
| **F10** | 250 ± 0.25 | 5.2 ± 0.25 | 4.1 ± 0.15 | 0.02 ± 0.21 |
| **F11** | 249 ± 0.34 | 5.3 ± 0.21 | 3.7 ± 0.21 | 0.35 ± 0.03 |
| **F12** | 250 ± 0.33 | 5.1 ± 0.14 | 3.5 ± 0.25 | 0.38 ± 0.24 |
| **F13** | 252 ± 0.24 | 5.2 ± 0.12 | 4.1 ± 0.12 | 0.09 ± 0.16 |
| **F14** | 248 ± 0.34 | 5.1 ± 0.21 | 4.2 ± 0.09 | 0.03 ± 0.18 |
| **F15** | 250 ± 0.36 | 5.2 ± 0.04 | 3.8 ± 0.18 | 0.18 ± 0.05 |
| **F16** | 249 ± 0.28 | 5.3 ± 0.06 | 4.1 ± 0.26 | 0.05 ± 0.21 |
| **F17** | 250 ± 0.25 | 5.2 ± 0.14 | 3.7 ± 0.17 | 0.23 ± 0.23 |
| **F18** | 252 ± 0.34 | 5.2 ± 0.16 | 3.9 ± 0.19 | 0.10 ± 0.21 |
| **F19** | 251 ± 0.37 | 5.0 ± 0.02 | 4.2 ± 0.16 | 0.03 ± 0.24 |
| **F20** | 249 ± 0.23 | 5.2 ± 0.07 | 4.5 ± 0.06 | 0.02 ± 0.02 |

Note: All values are expressed as mean±SD. n=3.

**Table No 9: Post compression evaluation parameter for orally disintegrating tablet of Mefenamic acid**

| Batch | Wetting time (s) | Water absorption ratio (%) | In vitro disintegration time (s) | Drug content (%) |
|---|---|---|---|---|
| **F1** | 23.12 ± 1.12 | 80.65 ± 2.00 | 21.08 ± 1.00 | 94.67 ± 1.53 |
| **F2** | 26.10 ± 1.23 | 82.45 ± 1.18 | 24.17 ± 1.12 | 92.45 ± 1.76 |
| **F3** | 19.34 ± 1.17 | 83.10 ± 1.23 | 16.14 ± 1.23 | 95.23 ± 1.35 |
| **F4** | 21.13 ± 1.08 | 81.32 ± 1.45 | 19.06 ± 1,17 | 94.10 ± 1.14 |
| **F5** | 20.08 ± 1.23 | 95.54 ± 0.23 | 14.04 ± 1.08 | 99.14 ± 0.89 |
| **F6** | 21.07 ± 1.15 | 92.35 ± 0.25 | 19.17 ± 1.16 | 96.28 ± 0.76 |
| **F7** | 26.45 ± 1.25 | 84.01 ± 1.23 | 24.35 ± 1.12 | 95.48 ± 1.68 |
| **F8** | 22.34 ± 1.18 | 87.34 ± 1.42 | 21.67 ± 1.18 | 94.67 ± 1.45 |
| **F9** | 28.32 ± 1.16 | 73.76 ± 2.12 | 26.43 ± 1.13 | 99.43 ± 1.67 |
| **F10** | 31.67 ± 1.19 | 74.43 ± 1.65 | 28.98 ± 1.00 | 101.89 ± 1.18 |
| **F11** | 27.32 ± 1.15 | 63.86 ± 1.34 | 25.20 ± 1.15 | 93.54 ± 1.53 |
| **F12** | 29.76 ± 1.27 | 65.43 ± 2.03 | 27.06 ± 1.19 | 99.76 ± 1.26 |
| **F13** | 32.43 ± 1.23 | 68.86 ± 0.89 | 30.43 ± 1.00 | 96.45 ± 1.90 |
| **F14** | 34.02 ± 1.26 | 64.43 ± 1.21 | 31.97 ± 1.12 | 102.87 ± 2.00 |
| **F15** | 31.09 ± 1.21 | 85.98 ± 0.45 | 29.54 ± 1.09 | 98.38 ± 0.67 |
| **F16** | 34.10 ± 1.27 | 82.65 ± 1.24 | 31.48 ± 1.05 | 99.98 ± 0.56 |
| **F17** | 32.56 ± 1.11 | 84.06 ± 1.32 | 28.97 ± 1.12 | 95.43 ± 1.35 |
| **F18** | 33.37 ± 1.18 | 89.84 ± 1.68 | 31.50 ± 1.16 | 91.29 ± 1.78 |
| **F19** | 32.96 ± 1.21 | 87.43 ± 1.47 | 30.12 ± 1.18 | 93.34 ± 1.90 |
| **F20** | 31.52 ± 1.23 | 85.21 ± 1.89 | 29.05 ± 1.04 | 94.90 ± 1.54 |

Note: All values are expressed as mean±SD. n=3.

**Table No 10: Post compression evaluation parameter for orally disintegrating tablet of Mefenamic acid**

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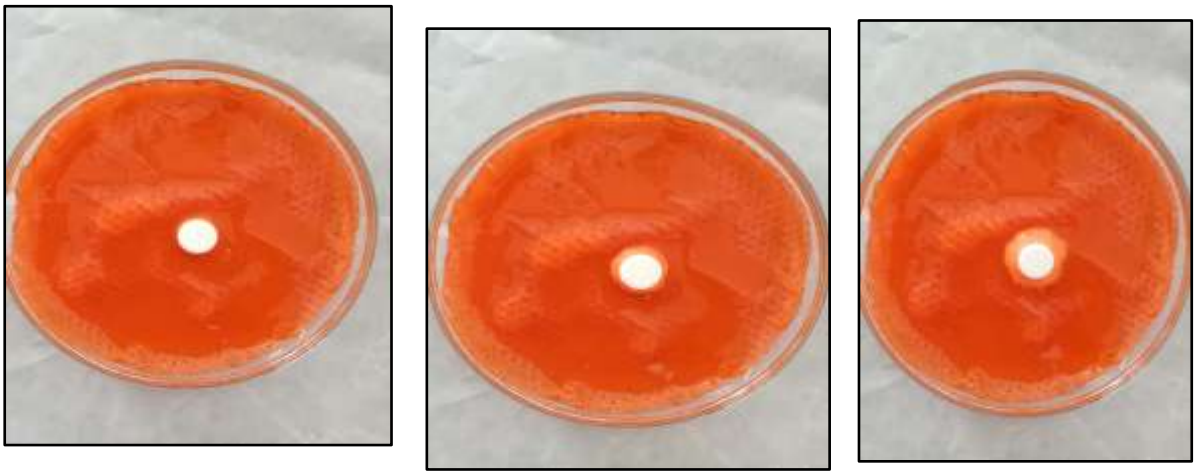

**1 Sec** **5Sec** **10 Sec**

**14 Sec** **16 Sec** **20 Sec**

**Fig No6: Wetting time of trial formulation F5 by Direct compression method**

**1Sec** **10 Sec** **15 Sec**

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**20 Sec** **25 Sec** **31 Sec**

**Fig No7: Wetting time of trial formulation F15 by Wet granulation method**

**In vitro dissolution studies:**

| Time (min) | F1 (%) | F2 (%) | F3 (%) | F4 (%) | F5 (%) | F6 (%) | F7 (%) | F8 (%) | F9 (%) | F10 (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| **5** | 11.09 | 16.05 | 14.65 | 20.45 | 38.64 | 43.67 | 25.78 | 24.87 | 31.78 | 37.98 |
| **10** | 15.07 | 21.98 | 18.67 | 27.67 | 47.37 | 57.89 | 30.41 | 27.46 | 38.67 | 41.89 |
| **15** | 18.54 | 27.65 | 22.87 | 30.32 | 58.14 | 68.90 | 37.86 | 32.57 | 42.89 | 53.41 |
| **20** | 22.89 | 34.76 | 27.45 | 35.67 | 69.34 | 73.56 | 45.67 | 41.67 | 50.54 | 60.87 |
| **30** | 28.33 | 39.65 | 36.78 | 39.89 | 76.45 | 79.98 | 49.80 | 45.83 | 57.98 | 71.32 |
| **45** | 39.33 | 42.78 | 40.89 | 43.65 | 87.64 | 83.67 | 54.79 | 57.67 | 64.54 | 78.83 |
| **60** | 41.45 | 44.54 | 47.78 | 52.46 | 95.89 | 87.43 | 60.65 | 72.78 | 77.86 | 82.09 |

**Table No11:In vitro dissolution studies (F1-F10) Orally disintegrating tablet of Mefenamic acid**

| Time (min) | F11 (%) | F12 (%) | F13 (%) | F14 (%) | F15 (%) | F16 (%) | F17 (%) | F18 (%) | F19 (%) | F20 (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| **5** | 12.67 | 23.67 | 27.76 | 13.41 | 43.31 | 28.98 | 18.67 | 21.34 | 28.67 | 32.56 |
| **10** | 32.56 | 29.98 | 54.65 | 24.65 | 47.87 | 31.39 | 23.34 | 32.96 | 32.65 | 48.96 |
| **15** | 57.54 | 34.54 | 58.12 | 31.36 | 56.40 | 42.59 | 35.98 | 43.56 | 38.76 | 53.98 |
| **20** | 69.86 | 40.63 | 62.14 | 39.90 | 61.98 | 48.42 | 43.54 | 56.09 | 43.54 | 62.54 |
| **30** | 73.31 | 47.98 | 71.43 | 41.58 | 72.43 | 53.32 | 52.76 | 63.95 | 51.23 | 75.43 |
| **45** | 78.84 | 53.31 | 76.65 | 52.98 | 80.12 | 67.90 | 63.98 | 70.32 | 67.78 | 82.97 |
| **60** | 80.14 | 61.45 | 82.12 | 58.12 | 85.09 | 74.63 | 66.89 | 82.98 | 85.34 | 90.45 |

**Table No 12 :In vitro dissolution studies (F11-F20) Orally disintegrating tablet of Mefenamic acid**

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**In vitro dissolution profile graph:**

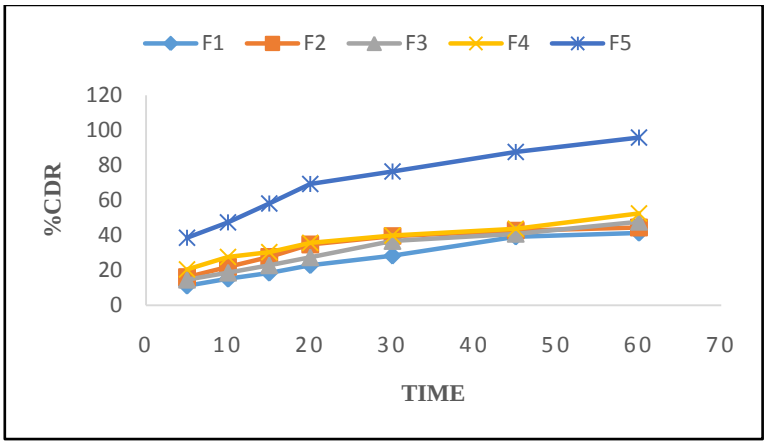


**Fig No8: In vitro dissolution graph F1-F5**

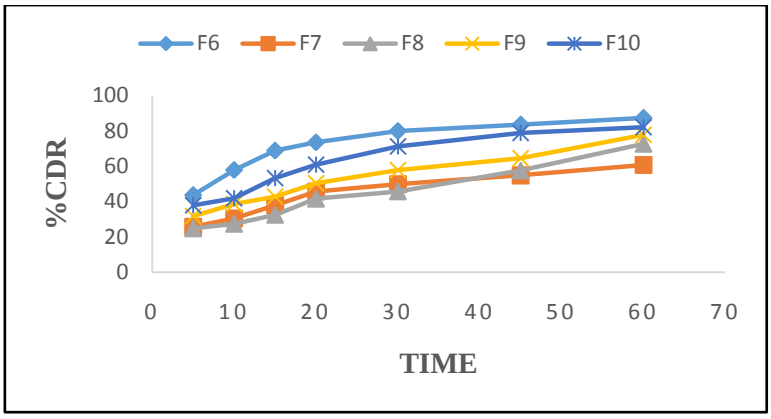


**Fig No9: In vitro dissolution graph F6-F10**

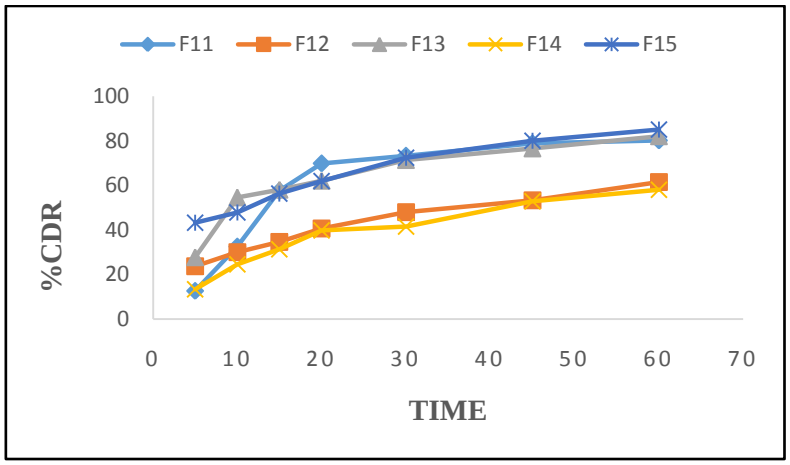


**Fig No10: In vitro dissolution graph F11-F15**

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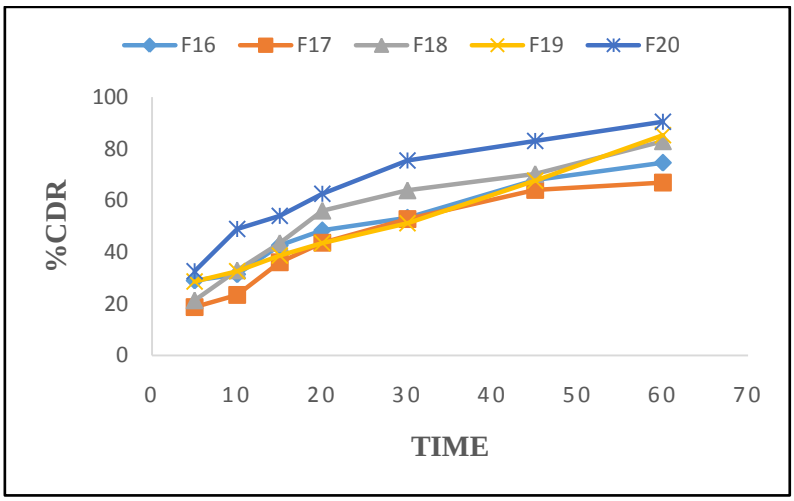


**Fig No11: In vitro dissolution graph F16-F20**

**Release Kinetic data of Optimized batch formulation:**

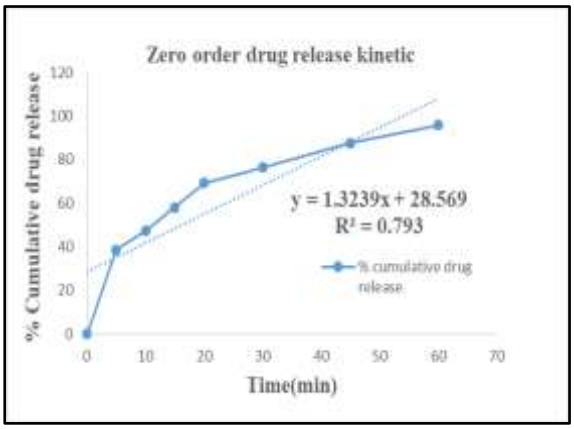


**Fig No12: Zero order model**

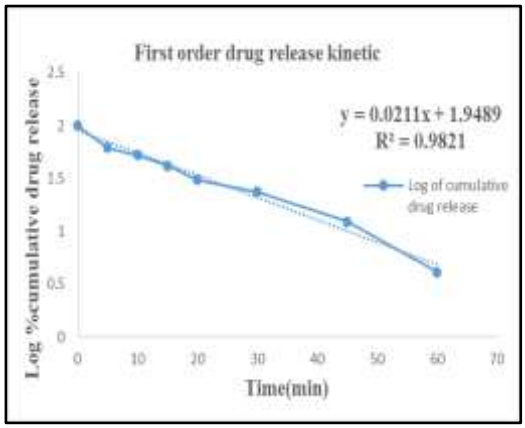


**Fig No13: First order model**

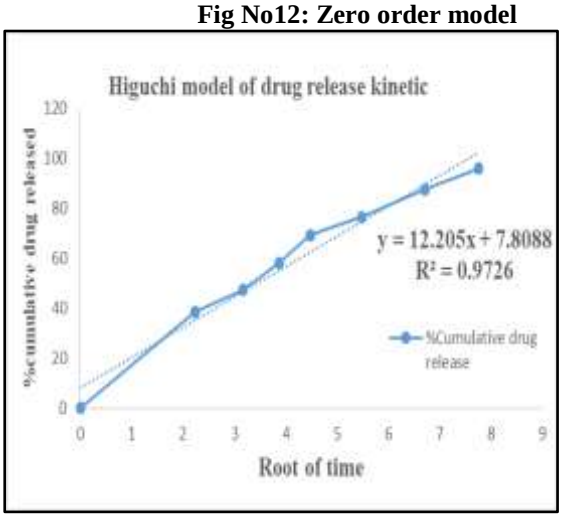


**Fig No 14:Higuchi model**

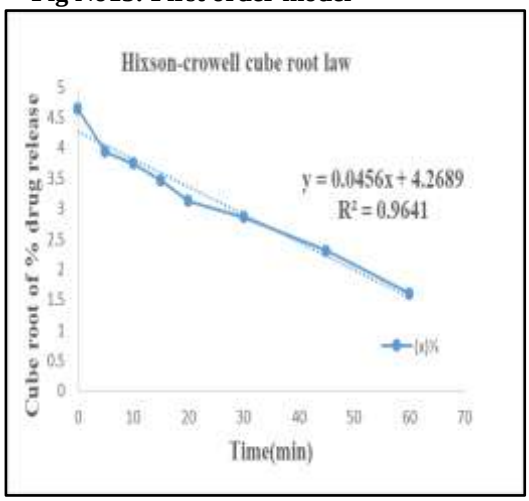


**Fig No15: Hixson- Crowellmodel**

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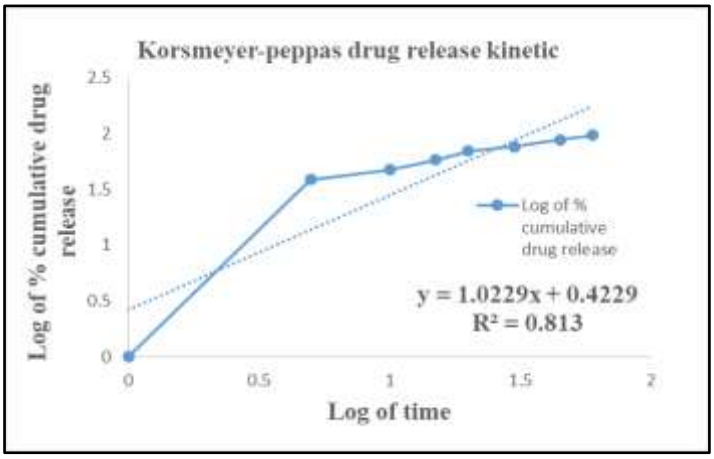


**Fig No16: Korsmeyer- peppas model**

**In vitro-Dissolution profile comparison:**

Optimized batch formulation of Orally disintegrating tablets of mefenamic acid were taken for comparison with marketed formulationDrug release profile of marketed product of mefenamic acid was determined and compared with the optimized formulation among the all batches, it can be concluded that tablet from optimized formulation showed more than 95.89% drug release within 60 minutes while marketed formulation showed about 96.34% drug release at the sametime, and nearly same drug release within 60minutes. The difference factor (F1) was found to be 4.42 and similarity factor (F2) was found to be 71.74 .Comparativedissolution profile of optimized batch formulation with marketed formulation is shown in Fig.No 13

| **Time (min)** | **Marketed formulation (MEFTAL-P) %CDR** | **Optimized batch formulation %CDR** |
|---|---|---|
| **5** | 34.18 | 38.64 |
| **10** | 49.98 | 47.37 |
| **15** | 61.58 | 58.14 |
| **20** | 70.54 | 69.34 |
| **30** | 83.97 | 76.45 |
| **45** | 89.45 | 87.64 |
| **60** | 96.34 | 95.89 |
| | | |
| **Difference factor (F1)** | 4.42 | - |
| **Similarity factor (F2)** | 71.74 | - |

**Table No 13:In vitro dissolution profile comparison between the marketed formulations with optimized batch formulation**

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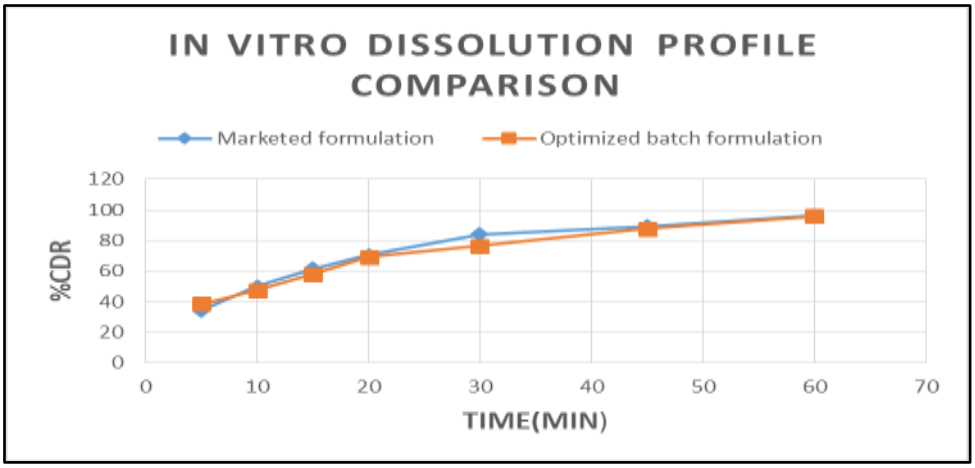


**Fig No17: In vitro-Dissolution profile comparison**

**Stability studies**

The stability studies as per ICH guidelines Q1 (A) of the optimized formulation at room temperature, 40℃/75%RH and 25℃/60% RH.

| parameter | Temperature and humidity condition | 1 month | 3 month |
|---|---|---|---|
| **Apperance** | 25℃ / 60%RH | White smooth surfaced on both side of tablet | White smooth surfaced on both side of tablet |
| | 40℃ / 75% RH | White smooth surfaced on both side of tablet | White smooth surfaced on both side of tablet |
| | Room temperature | White smooth surfaced on both side of tablet | White smooth surfaced on both side of tablet |
| **Uniformity weight (mg)** | 25℃ / 60%RH | 250 ± 0.23 | 250 ± 0.06 |
| | 40℃ / 75% RH | 251 ± 0.45 | 250 ± 0.12 |
| | Room temperature | 250 ± 0.65 | 251 ± 0.18 |
| **Hardness ( $kg/cm^2$)** | 25℃ / 60%RH | 3.4 ± 0.12 | 3.2 ± 0.34 |
| | 40℃ / 75% RH | 3.2 ± 0.54 | 3.1 ± 0.72 |
| | Room temperature | 3.2 ± 0.03 | 3.2 ± 0.32 |
| **Wetting time(s)** | 25℃ / 60%RH | 21.08 ± 0.23 | 20.08 ± 1.23 |
| | 40℃ / 75% RH | 19.08 ± 0.33 | 21.08 ± 0.23 |
| | Room temperature | 20.08 ± 1.23 | 19.18 ± 0.63 |
| **In vitro disintegration time (s)** | 25℃ / 60%RH | 14.34 ± 0.08 | 14.03 ± 1.08 |
| | 40℃ / 75% RH | 15.04 ± 1.05 | 15.34 ± 0.81 |
| | Room temperature | 14.02 ± 0.28 | 14.04 ± 0.81 |
| **Drug content (%)** | 25℃ / 60%RH | 99.54 ± 1.89 | 98.14 ± 0.09 |
| | 40℃ / 75% RH | 98.14 ± 0.89 | 99.14 ± 0.19 |
| | Room temperature | 99.64 ± 0.59 | 98.54 ± 0.94 |
| **In vitro drug release (min)** | 25℃ / 60%RH | 94.29±0.75 | 95.35±0.05 |
| | 40℃ / 75% RH | 95.58±0.25 | 94.05±0.47 |
| | Room temperature | 95.34±0.28 | 95.89±0.45 |

**Table No 14: Stability studies of orally disintegrating tablet**

## IV. CONCLUSION

Difficulty in swallowing tablet is a major problem especially for patients suffering from geriatric and pediatric, psychiatric patients .In the present work, orally disintegrating tablet of mefenamic acid were prepared by direct compression method using different concentration of , Natural superdisintegrents , Effervescent agent,

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Saliva activating agent, Diluent, lubricant, Glidant, Taste masking agent ,Sweetening agent were optimized.The comparison between the direct compression and wet granulation method for formulation of orally disintegrating tablets.showes better optimized batch F5 of direct compression.The dissolution profile of optimized formulation was compared with that of the marketed orally disintegrating tablet. Optimized formulation showed satisfactory results in pre and post compression characterization parameter.The stability studies as per ICH guidelines Q1 (A) of the optimized formulation at room temperature, 40℃/75%RH and 25℃/60% RH showed no substantial changes in physical characteristics and dissolution profile of the tablets.

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