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# FORMULATION AND EVALUATION OF DISPERSIBLETABLET OF CIMETIDINE

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**ABSTRACT:** -The utilization of fenugreek gum, a naturally occurring super disintegrant, in developing a fast-acting cimetidine drug delivery system, was investigated. A thorough physicochemical investigation was performed on the extracted gum. An Electro Lab Dissolution Tester USP II (USP Dissolution Apparatus Type II) running at 50 rpm, 37 ± 0.5°C, and 900 ml of medium volume was used for an in vitro drug release investigation. F3 performed better than the other tested formulations, reaching a maximum drug release of 98% in 25 minutes. This finding emphasizes fenugreek gum's potential as a useful ingredient for quickly dissolving prescription pills. The findings add to continuing efforts to use natural and biocompatible materials in improving drug delivery systems by supporting more research andpossible clinical applications.

**Keywords:** - Fenugreek gum, Super disintegrant, Cimetidine drug delivery, In vitro drugrelease, Biocompatible materials

## • INTRODUCTION

The idea behind the fast-dissolving pills was to provide patients with a more traditional way to take their medication. Due to physiological changes, patients of all ages have dysphasia, which is the inability to swallow, particularly in the elderly and pediatric population. Fast-dissolving tablet dose forms that dissolve, dissolve, or suspend with saliva in the mouth for easy swallowing benefit many patients, including pediatric and geriatric patients and adult patients who prefer the convenience of readily swallowable dosage forms. This tablet dissolves quickly on the tongue, releasing the drug with a pH of 6.8 dissolves or disperses in saliva. [1].

Two types of dispersible tablets need to be distinguished: one kind dissolves in the mouth instantaneously, so the patient may take it without needing water, and the other type of pill dissolves readily in water and can be absorbed by the patient. [2]. "Fast dissolving" is defined by the European Pharmacopoeia as tablets that should dissolve on the tongue in less than three minutes after ingesting. [3] The most common dose type is a solid one, but its primary

disadvantage is dysphagia, or trouble swallowing. Due to this issue, new solid dosage forms were created, such as fast-dissolving tablets, which dissolve quickly in saliva and don't require water. Drug administration that dissolves quickly (fast-dissolving tablets) prevents first-pass metabolism and increases the active ingredient's bioavailability. [4]

- **Need for fast-dissolving tablets:** Rapid-dissolving delivery systems are in demand because of patients' low acceptability and compliance with present distribution regimens, drug manufacturers' constrained market price, and the high cost of sickness management.
- **Effectiveness factor:** Enhanced solubility, quicker start of action, and enhanced bioavailability are the main marketing points of these dosage forms. Tablet formulations are disseminated insaliva within the oral cavity and might cause pre-gastric absorption when the medication dissolves quickly.
- **Limitation of fast dissolving tablets:** Certain medications, such as antibiotics like ciprofloxacin, should be associated withbigger dosages since they might be challenging to manufacture for FDT.

**1.** An adult dose tablet of the medication contains around 500 mg.

**2.** Orally disintegrating pills might not be the best choice for patients who also use anticholinergic drugs. Similarly, these pill formulations might not be appropriate for persons with Jorgen's syndrome or dry mouth from diminished salivary flow.[5]

➢ **Selection of Ideal Drug Candidates of fast Dissolving Tablets:**

- The dosage of fast-dissolving tablets needs to be less than 20 mg.
- The medication has to be somewhat non-ionized at the oral cavity's pH. [5]

➢ **Technology for fast-dissolving tablets:**

**1.** **Freeze-drying or lyophilization:** Freeze drying, often referred to as lyophilization, is the process of removing solvent froma frozen pharmaceutical solution or suspension, including excipients that contribute to structure. When saliva comes into touch with the new, rapidly dissolving tablets made using freeze-drying technology, they dissolve and break down rapidly due to their high porosity.

One major benefit of this technology is that the freeze-dried dosage form hascomparatively fewer stability issues throughout its half-life when stored in a dried condition. The primary purpose of this freeze-drying method is for medications that are heat-sensitive, or thermolabile.

2. **Sublimation:** Compressing the mixture into a tablet after adding inert volatile chemicals to other excipients, such as urea, urethane, naphthalene, camphor, etc., is one way to dissolve tablets quickly.

3. **Spray drying:** This method uses sodium starch glycolate and crosspovidone as super disintegrants, mannitol as a bulking agent, and both hydrolyzed and unhydrolyzed gelatin as a matrixand supporting agent. It has been claimed that tablets made from spray-dried powder dissolve in aqueous medium in less than 20 seconds. [6]

4. **Direct compression:** This method is a simple way to create quickly dissolving tablets since it requires few processing stages and has extremely cheap manufacturing costs. Direct compressed tablet disintegration and dissolution are influenced by effervescent agents, water-soluble excipients, and distinct disintegration effects. The ideal kind and concentration of disintegration should be chosen to achieve quick disintegration and high dissolving rates.

5. **Melt granulation technology:** Super polystrate technology was combined with the melt granulation method to create fast-dissolving tablet formulations. This method allows the material to form granules when it is molten. The formulation also contained mannitol as a water-soluble excipientand crosscarmellose sodium as a disintegrating agent. Crystallized paracetamol was utilized as the model medication. [7]

- **Patented Technology:**

1. **Zydis Technology**: Pharmaceutical companies have never before offered fast-dissolving tablet dosage formulations as a result of this method. It contains a special type of freeze-dried tablet where the active ingredient is mixed with a water-soluble matrix, shaped into blisterpockets, then freeze-dried to eliminate water by sublimation. The zydis matrix is composed of several components designed to achieve different objectives. Polymers such as gelatin, dextran, or alginates are addedto enhance strength during handling.

2. **Orasolv Technology (Cima Labs):** The CIMA lab has patented this technique. These technologies involve the formulation of the FDTs using effervescent disintegrating agents squeezed at low pressure. Fizzing sensations are produced by the carbon dioxide evolving out of the tablet, a favorable organoleptic feature. The effervescent mixture is usually administered at a dosage of 20– 25% of the total weight of the pill. Be5. cause there is little compressive force used in their construction, tablets are naturally soft and fragile.

3. **Frosta Technology (Akina):** Making plastic granules and crushing them under low-pressure results in strong tablets with high porosity. Plastic granules are made of a binder,

an enhancer of water penetration, and a porous plastic substance. Depending on the size of the tablet, the resulting tablets have a fast disintegration time of 15 to 30 seconds and exceptional hardness. Filler lowers the porosity of tablets, which lowers the rate of disintegration.

4. **QUICKSOLV Technology:** The Quicksolv matrix compositions include dissolving these formulations in the solvent, usually water, and freezing the resulting solution. At that temperature, the first solventwill still be solid, and the frozen solution will then come into contact with the second solvent, which is often menthol, acetone, or ethanol.

   Therefore, the first solvent is removed a few hours after coming into contact with the second solvent to form a functional matrix. The completed product crumbles easily. It is claimed that this method has uniform porosity, enough handling strength, and the capacity to reduce or eliminate the likelihood of cracking during the last preparation.

5. **LYCO Technology:** Despite using a similar process to Zydis, Lyco Technology's product is frozen while it is kept on the shelves of the freeze dryer. For these tablets to be formulated, a significant amount of undissolved inert filler, such as mannitol, is also needed to make the process solution more viscous and to keep homogeneity from being sedimented. Denser tablets dissolve at speeds similar to the loosely compressed quick melt formulations when a large filler content is used to lower the dry dosage form's potential porosity.

- **Super disintegrants:** For the purpose of to aid in the disintegration of the compacted mass in a fluid environment, disintegrating agents are frequently included to tablet formulations. They facilitate the tablet matrix's dispersion and moisture penetration. Super disintegrants are substances added to some encapsulated formulations and tablets to cause the "slugs" to disintegrate into smaller bits in an aqueous environment.

  This accelerates the release of the therapeutic ingredient and increases the surface area that is accessible. They facilitate the tablet matrix's dispersion and moisture penetration. The disintegration of tablets has drawn a lot of attention as a crucial step in achieving rapid medication release. The focus on medication availability draws attention to how crucial it is for a tablet to dissolve reasonably quickly to guarantee unrestricted drug-dissolving behavior.[8]

- **Mechanism of super disintegrants:**

1. **Swelling**: Swelling is thought to be a process by which some disintegrating substances (like starch) transfer the disintegrating effect, even though not all effective disintegrants expand

when they come into contact with water.

2. **Porosity and Capillary Action (Wicking):** It is thought that porosity and capillary action transfer the disintegration activity of effective disintegrants that do not swell. Tablet porosity creates spaces for liquid to seep into tablets.
   These paths into the tablet are made possible by the disintegrant particles, which operate to promote porosity due to their poor cohesion and compressibility. Through capillary action, liquid is "wicked" or pulled up into these routes, rupturing the interparticulate connections and causing the tablet to shatter apart.

3. **Deformation**: It is believed that the disintegration activity of efficient disintegrants that do not swell is transferred by porosity and capillary action. Tablet porosity creates spaces for liquid to seep into tablets. These paths into the tablet are made possible by the disintegrant particles, which operate to promote porosity due to their poor cohesion and compressibility. Through capillary action, liquid is "wicked" or pulled up into these routes, rupturing the interparticulate connections and causing the tablet to shatter apart.

- **Type of Superdisintegrant:**
- **Natural Superdisintegrant:**

1. **Fenugreek gum -** Trigonella foenum graecum, often referred to as fenugreek, is an annual plant that belongs to the Leguminosae family. It is the well-known spice used in human cuisine. Fenugreek has long been employed in medicine and food preparation; its green leaves and seeds are utilized for both purposes.
   It has been used to alter the texture and enhance the flavor and color of culinary items. Fenugreek seed has several therapeutic uses, including lowering cholesterol, helping with breastfeeding, fighting bacteria, stimulating the stomach, treating anorexia, acting as an antidiabetic, galactagogue, hepatoprotective, and have anticancer effects. [9]
2. **Fenugreek gum (seed): -** Fenugreek is known for its pleasantly bitter, slightly sweet seeds. The seeds are used to flavor a variety of meals, primarily curry powders, teas, and ice blends. The center of a fenugreek seed is a firm, yellow embryo, surrounded by a rather thick coating of white, semi-transparent endosperm.

   Using the free-radical scavenging technique, the extracts of endosperm husk and fenugreek seed at concentrations of around 200 g showed antioxidant activity of 72%, 64%, and 56%, respectively. [9]

- **Synthetic Super disintegrants:**

1. **Sodium starch glycolate:** While many other native starches may be utilized to produce sodium starch glycolate, potato starch is often employed since it has the finest disintegration qualities phosphorus oxychloridein alkaline solution or sodium tri metaphosphate.

2. **Cross-linked polyvinylpyrrolidone (crospovidone):** Crospovidone super disintegrants employ a mix of methods for disintegration, in contrast to conventional super disintegrants that primarily rely on swelling.

   Crospovidone quickly draws saliva into the tablet, generating the hydrostatic pressures and volume expansion necessary for a quick breakdown in the mouth. Despite other super disintegrants that largely rely on swelling for disintegration, crospovidone super disintegrants use both swelling and wicking in addition to swelling.

- **APPROACHES FOR FAST DISSOLVING TABLETS [8]**

  Various approaches to formulate fast-dissolving tablets can be possible, which arediscussed under

1. **Lyophilization or Freeze-drying Freeze drying (Lyophilization):** One major benefit of the freeze-drying approach is that it operates at room temperature the whole time, preventing any negative thermal effects that may compromise the stabilityof the medicine throughout processing. The lyophilized product imparts a glassy amorphous form, which may increase the drug's dissolving characteristics.
2. **Molding**: Water-soluble compounds usually make up the majority of the components in molded tablets. Using this technique, a solvent (often ethanol and water) is used to moisten the powder combination, which is then crushed onto mold plates to create a wetted mass (compression molding).
3. **Direct compression**: Fast-dissolving tablet production with a normal tablet press is an appealing approach since it provides easy technology transfer and inexpensive manufacturing costs. Other benefits include a low number of processing stages and widely accessible excipients.

   These dosage forms can accommodate high doses. In the direct compression approach, disintegrants, water-soluble excipients, and effervescent agents work individually and in concert to facilitate the disintegration and solubilizationof tablets.

- **METHODS FOR PREPARING SOLID SOLUTIONS**

1. **Kneading Technique:** This process turns the carrier into a paste by allowing water toseep through. After that, the drug is added and kneaded for a set amount of time. After kneading, the mixture is dried and, if needed, sieved.
2. **Solvent evaporation method:** In this procedure, an organic solvent is used to dissolve the medication and carrier. The solvent evaporates after the whole dissolution is complete. The solid material is dried, sieved, and ground. Ex: Using the solvent evaporation process, a solid furosemide and eudragits dispersion was created
3. **Co-precipitation method:** The appropriate quantity of medicine is added to the carrier solution. The system is maintained in a state of magnetic agitation and is shielded from light. The resulting precipitate is vacuum-filtered and allowed to dry at room temperature to preserve the structural water of the inclusion complex.
4. **Melting method:** A mortar and pestle are used to combine the drug and carrier. To get a homogenous dispersion, the mixture is heated to each component's melting point or above.

   After that, it cools to form a solidified lump. After crushing, it is sieved. Using this technique, urea and albendazole solid dispersion was created, for example.[10]

## ➢ Material and Method

**Table No. 1: List of Instruments**

| S. No. | Instrument Used | Make/ Model Name |
|---|---|---|
| 1. | UV Spectrophotometer | Schimadzu 1800 |
| 2. | Melting point apparatus | Remi Pvt. Ltd. |
| 3. | Dissolution Test Apparatus | Electro lab Pvt. Ltd. |
| 4. | Hardness Tester | Monsento Labs Pvt. Ltd. |
| 5. | Friability Apparatus | Scientech Pvt. Ltd. |
| 6. | Disintegration Test Apparatus. | Scientech Pvt. Ltd. |
| 8. | Hot air Oven | S.M. scientific instrument (p) Ltd. |
| 9. | Tablet Compression Machine. | Aidmach Pvt. Ltd. |
| 10. | Weighing balance | Shimadzu |
| 11. | pH – Meter | MK VI |
| 12. | Bulk Density Apparatus | Scientech Pvt. Ltd. |

**Figure: -1 List of Materials and their uses**

| S. No. | Material | Manufacturer Name | Uses |
|---|---|---|---|
| 1 | Cimetidine | Yarrow Chem Pvt. Ltd. | Active Pharmaceutical Ingredient (API); gastric acid reducer |
| 2 | Fenugreek seeds | Yarrow Chem Pvt. Ltd. | Natural superdisintegrant for fast dissolving tablets |
| 3 | Sodium Starch Glycolate | Lobachem Pvt. Ltd. | Superdisintegrant for rapid tablet disintegration |
| 4 | Croscarmellose Sodium | Lobachem Pvt. Ltd. | Superdisintegrant for tablet disintegration |
| 5 | Microcrystalline cellulose | Lobachem Pvt. Ltd. | Binder and filler in tablet formulations |
| 6 | Magnesium Stearate | Lobachem Pvt. Ltd. | Lubricant to aid tablet manufacturing |
| 7 | Talc | Lobachem Pvt. Ltd. | Glidant and lubricant in tablet production |
| 8 | Mannitol | Lobachem Pvt. Ltd. | Binder and sweetener in tablet formulations |

- **Extraction and purification of fenugreek gum:** [15] A lab mill was used to grind 100 g of fenugreek seeds to a mesh size of 100. Boiling hexane was used in a soxhlet system to extract the fine powder for 80 minutes. To get rid of the undesirable saponins, the extracted material was treated with 95% ethanol for 130 minutes in a conical flask while preserving its boiling temperatures. To deactivate additional enzymes, reflux the extract with 70% ethanol for 180 minutes. If required, ethanol was applied to the refluxing mixture many times to get rid of any remaining residues. At room temperature, the residue was filtered through sintered glass. For eight hours, the filtered residue was mechanically stirred at 700 rpm while water was added. The resulting mixture was centrifuged for 12 minutes at 100C at 5000 rpm. Crude fenugreek gum was found in the supernatant, which was decanted and precipitated by adding 70% ethanol. As a result, acetone, diethyl ether, and water were used to wash the gum precipitate. The pure gum fenugreek was dried in an oven. At room temperature, the residue was filtered through sintered glass. For eight hours, the filtered residue was mechanically stirred at 700 rpm while water was added. The resulting mixture was centrifuged for 12 minutes at 100C at 5000 rpm.Crude fenugreek gum was found in the supernatant, which was decanted and precipitated by adding 70% ethanol.

➢ **Physicochemical characterization of fenugreek gum:** The solubility, swelling index, and drying loss of the extracted gum powder were assessed after it had been dried and purified**.**

1. **Solubility Study**: The solubility of fenugreek gum powder was determined in an aqueous medium (different temperature) and organic solvent.

2. **Swelling index:** A graduated cylinder with a stoppered capacity of 100 mL was used for the investigation. One gram of fenugreek gum's initial bulk volume was recorded. After vigorously shaking every 10 minutes for an hour, enough water was added to guarantee 25 mL of equal dispersion. The mixture was then left to stand for 24 hours. After 24 hours, the sediment volume of the enlarged mass was measured while the dispersion was kept at room temperature.

**Swelling index = 100 [(V2-V1) / V1]**

3. **Loss on drying:** The loss-on-drying approach is a useful tool for identifying excessive moisture or solvent content in a sample. The material sample (W1) was weighed and cooked to 400C±20C in an oven for two hours. After cooling in the desiccator's dry environment, it was weighed at the end (W2).

**% Loss on drying= [(W1-W2)/W1] 100**

- **Preformulation Study: -**

- **Identification of Drug:**

1. **Authentication of drug sample by U.V. Spectrophotometer:** 50mg of drug was weighed and dissolved in 50ml of methanol (1mg/ml). 10ml of this solution was withdrawn and volume was made up to 100ml. Methanol was used to make the proper dilutions to achieve a concentration of 10 µg/ml. Then, the UV spectra were captured and scanned in the 200–400 nm region. [11]

2. **Authentication of drug sample by FTIR:** Fourier Transform Infrared spectroscopy (FTIR) Spectrum was recorded of pure samples were analyzed by KBr pellet method using FTIR spectroscopy. About 10 mg of Cimetidine mixed with potassium bromide of equal weight. The spectra were scanned over a frequency range of 4000 -400 $cm^{-1}$.[1]

3. **Differential Scanning Calorimetry:** The thermogram of pure cimetidine acquired by DSC (mettle star 8.10) at a heating rate of 100C/minute across a temperature range of 35–3000C is known as the DSC of Cimetidine.

   A 2.0 mg sample that was precisely weighed was hermetically sealed in an aluminum pan. To keep the environment inert, 10 milliliters of nitrogen gas were purged every minute.[35]

4. **Drug-excipient interaction study:** The drug-excipient interaction research was used to evaluate the drug's compatibility. The medication was combined in glass vials with different excipients in a 1:1 ratio, sealed tightly, and stored at 40°C for 14 days without being disturbed. TLC verified any incompatibility after 14 days.[12]

- **Preparation of Cimetidine Fast-dissolving tablets**

1. **Direct Compression Method.** Weighed all Ingredients as per the quantities. Pass all the ingredients through sieve #80 and collect individuals in polybags. The combination of fenugreek gum, sodium starch glycolate, croscarmellose sodium, microcrystalline cellulose, and mannitol in a specified amount.

   Magnesium stearate and talc was added to it and blend for 5 min in a pestle mortar. Utilizing D-Tooling's multiple rotatory compression machine with 10 mm round punches and matching dies, compress the final mix.

**Table No. 2: Composition of Cimetidine Fast Dissolving Tablets.**

| S.No | Ingredients | Formulation Code (quantity in mg) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
| 1. | Cimetidine | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| 2. | Fenugreek Gum | 7.5 | 10 | 12.5 | - | - | - | - | - | - |
| 3. | Sodium Starch Glycolate | - | - | - | 7.5 | 10 | 12.5 | - | - | - |
| 4. | Croscarmellose Sodium | - | - | - | - | - | - | 7.5 | 10 | 12.5 |
| 5. | Microcrystalline cellulose | 86.5 | 84 | 81.5 | 86.5 | 84 | 81.5 | 86.5 | 84 | 81.5 |
| 6. | Mannitol | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| 7. | Magnesium stearate | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| 8. | Talc | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| **Total Weight (in mg)** | | **350** | **350** | **350** | **350** | **350** | **350** | **350** | **350** | **350** |

- **EVALUATION PARAMETER:**

- **Evaluation of Precompression Parameter of Fast Dissolving Tablets:** [13,14]

1. **Angle of repose:** The angle of repose of the powder blend was determined using the funnel technique. The powder combination was weighed properly and then put into a funnel. That

is the height at which the funnel was kept in contact with the powder blend heap. The powder mixture was supposed to freely pour onto the surface through the funnel.

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

2. **Bulk Density:** The mass of the powder divided by the bulk volume is known as the bulk density, or ρb, and it is represented in g/cm3.[18]

$$P_b = M / V_b$$

3. **Tapped Density:** It is the proportion of the powder's total mass to its tapped volume. The powder blend was tapped fifty times to determine the volume. After that, the tapping was done 50 times, and the loudness was recorded. To calculate taped density, the following formula was used:

$$P_t = M / V_t$$

- **Evaluation of Post compression Parameter of Fast Dissolving Tablet:**

4. **Thickness:** Twenty tablets were chosen at random from the formulation, and each tablet's thickness was measured using a screw gauge. The result was expressed in millimeters.

**Thickness= weight of tablet/Area of tablet**

5. **Hardness:** The Monsanto hardness tester has a "0 to 20" kilogram range. The amount of force required to break the tablet was recorded as the screw knob was cranked forward. Three tablets were randomly tested for each formulation batch, and the average reading was recorded. It is represented as kg/cm2 [19].

**Hardness= Force required to break the tablet / Surface area of the tablet**

6. **Weight variation:** Twenty tablets were randomly taken from each batch and the weight of their average weight was determined. The individual weight was compared with the average weight. The weight was measured using a weighing balance.[20]

7. **Friability:** A friability test was performed by using a Roche friability. The friability was filled with ten weighted tablets and turned on at a speed of twenty-five revolutions per minute. Following four minutes (i.e., 100 rotations), the tablets were cleaned and weighed again. This formula was used to determine the percentage of friability. [21]

**Percentage friability = Initial weight - Final weight / Initial weight ×100** [21]

8. **Wetting time:** Two layers of tissue-adsorbent paper that were put into a Petri dish had the tablet positioned in the middle of them. The extra water was fully drained from the dish after

the paper had been properly wetted with distilled water.

Then, using a timer, the amount of time needed for the water to diffuse from the wetted absorbent paper across the whole tablet was noted.

9. **Water absorption ratio:** The piece of tissue adsorbent paper was folded twice was placed in a small petri dish containing 6 ml of water. On the tissue paper, a tablet was placed and given time to get soaked. Once more, the pill was moistened and weighed. Using the following equation, the water absorption ratio, or R, was calculated.[22]

$$R = 100 \times (W_a - W_b)/W_a$$

$W_a$ = Weight of tablet after water absorption $W_b$ = Weight of wetted tablet before water absorption [3]

10. **Drug contents:** The amount of medication included in each formulation was ascertained by taking twenty pills. Using a mortar and pestle, the pill was ground into a powder, and the resulting mixture was then transferred into a standard flask with a capacity of 100 milliliters. The powder was dissolved in five milliliters of methanol and then filled with a pH 6.8 phosphate buffer. After the material was well combined, it was filtered using membrane filter paper with a 0.45-micron size. [23]

11. **In vitro Disintegration Test:** The USP disintegration test apparatus was used to determine disintegration time. In 900 ml of water at 370C, six tablets from each formulation were tested. The study was done in triplicate. [3]

12. **In vitro Drug release study:** Using an Electro Lab Dissolution Tester USP II (USP Dissolution Apparatus Type II) at 50 rpm, 37±0.5 0C, and 900 ml of medium, the in vitro dissolution research of designed fast dissolving tablets F1–F9 was conducted. Throughout the investigation, a constant temperature of 37±0.5 0 C was maintained.

    For this experiment, phosphate buffer (900 ml, pH 6.8) served as the dissolving media. At predetermined intervals, five milliliters of the material were extracted and subjected to analysis at 237.80 nm using a UV spectrophotometer (Shimadzu 1800, Japan). The USP paddle-type dissolving equipment was used to evaluate the impact of drug release in fast-dissolving tablets. The sample was measured by a UV spectrophotometer (Shimadzu 1800, Japan) at 273.80 nm at specified intervals. [24]

13. **Stability studies**: In the stability chamber, the stability investigations were conducted for one month. As directed by the ICH recommendations, the tablets were kept at 40°C±2°C and

75±5% relative humidity, Q1C. Every thirty days, the pills were taken out and examined for things like hardness, medication content, disintegration, and wetting time.[25]

## ➢ RESULT AND DISCUSSION:

- **Fenugreek gum extraction and purification**: Fenugreek gum was taken out of the seed.
- **Characterization of Fenugreek gum:** The purified and dried extracted gum powder was evaluated for its micrometric properties' pre-formulation studies, solubility studies, swelling index, and loss on drying.

**Table No. 3: Physicochemical characterization of fenugreek gum:**

| S.No. | Parameters | Result (n=3) |
|---|---|---|
| 1 | Loss on drying | 5%±0.611 |
| 2 | Swelling index | 133%±0.650 |
| 3 | Solubility | Slightly soluble in cold water and insoluble in organic solvents |
| 4 | Bulk density | 0.769±0.023g/ml |
| 5 | Tapped density | 0.909±0.005g/ml |
| 6 | Compressibility index | 15.40 %±0.511 |
| 7 | Hausner's ratio | 1.18±0.611 |
| 8 | Angle of repose | $19.20^0$±0.650 |
| 9 | Percentage Yield | 27 %±0.221 |

## ➢ PREFORMULATION STUDY:

## ➢ Identification and Drug Characterization

- **Determination of Maximum wavelength using UV spectrophotometer:**

The maximum wavelength of Cimetidine was found to be 237.80. nm which matches the

reported wavelength.

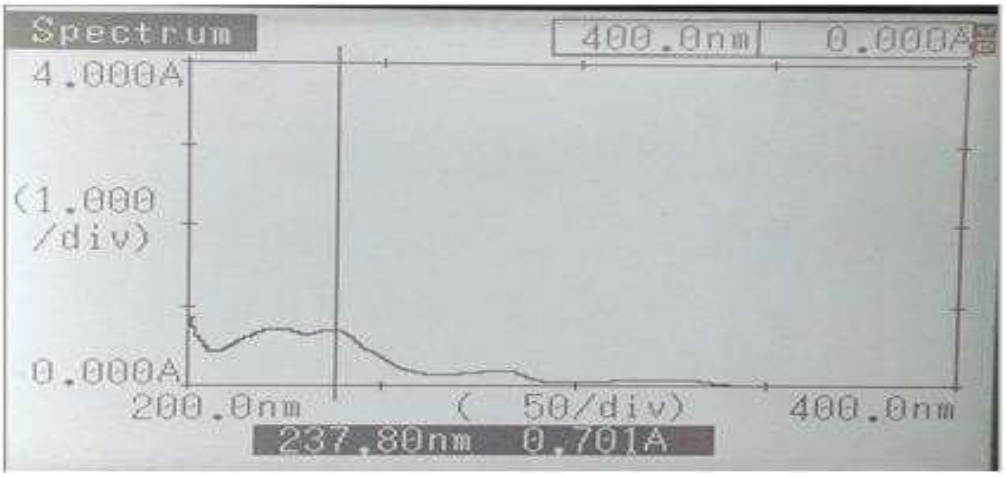


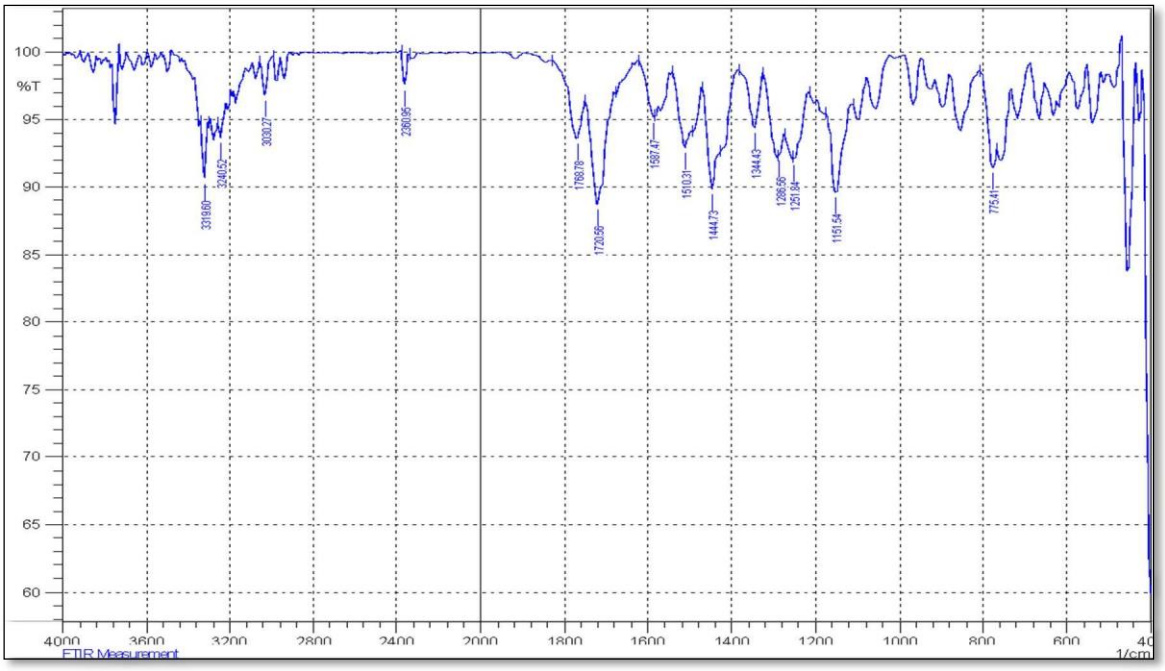

**Figure 2 : UV Spectrum of Cimetidine in ethanol**

- **Authentication of drug sample by FTIR Spectroscopy:**
- **FTIR:** (Fourier Transform Infrared Spectroscopy) The prominent IR absorption peak of Cimetidine at 3319.60 and 3240.52that these broad peaks may be due to OH hydrogen bonding. 1766.76 and 1720.56 carbonyl group vibration. 1587.47 indicate the presence of C=C ring stretching and 1510.31 N-H bending presence in the FTIR of Cimetidine.

| S. No. | Reference reading | IR Absorption peak | Chemical group |
|---|---|---|---|
| 01 | 3000-3500 | 3319.60 | OH hydrogen bonding |
| 02 | 3200-4000 | 3340.52 | OH hydrogen bonding |
| 03 | 1500-2000 | 1766.76 | Carbonyl group |
| 04 | 1500-2000 | 1720.56 | Carbonyl group |
| 05 | 1500-1700 | 1510.31 | NH group |
| 06 | 1500-1700 | 1587.47 | C=C group |

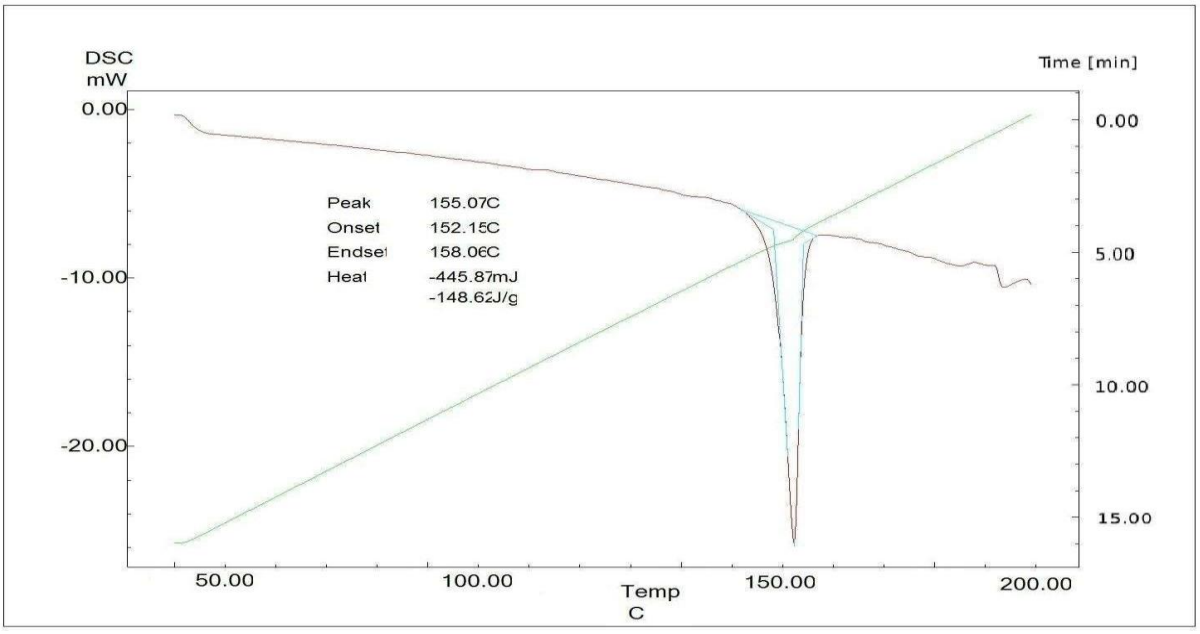
**Table No. 4 : FTIR Spectra of Cimetidine**

**Figure: 3 FTIR Spectra of Cimetidine**




- **Differential Scanning Calorimetry:** the DSC thermogram of Cimetidine exhibited endothermic peak at 155.07 $^{0}$ C which corresponds to the melting point of Cimetidine

**Figure 4: DSC graph of Cimetidine.**




- **Preparation of calibration curves:** The calibration curves of Cimetidine in various solvents

e.g. Distilled water, and 6.8 pH phosphate buffers were prepared and shown in Table No. 5.

**Table No. 5: Absorbance data of Cimetidine in distilled water for preparation of calibration curve, at 237.80 nm.**

| S. No. | Concentration (µg/ml) | Absorbance (n=3) |
|---|---|---|
| 1 | 2 | 0.066±0.1 |
| 2 | 4 | 0.125±0.6 |
| 3 | 6 | 0.198±0.3 |
| 4 | 8 | 0.256±0.1 |
| 5 | 10 | 0.331±0.2 |

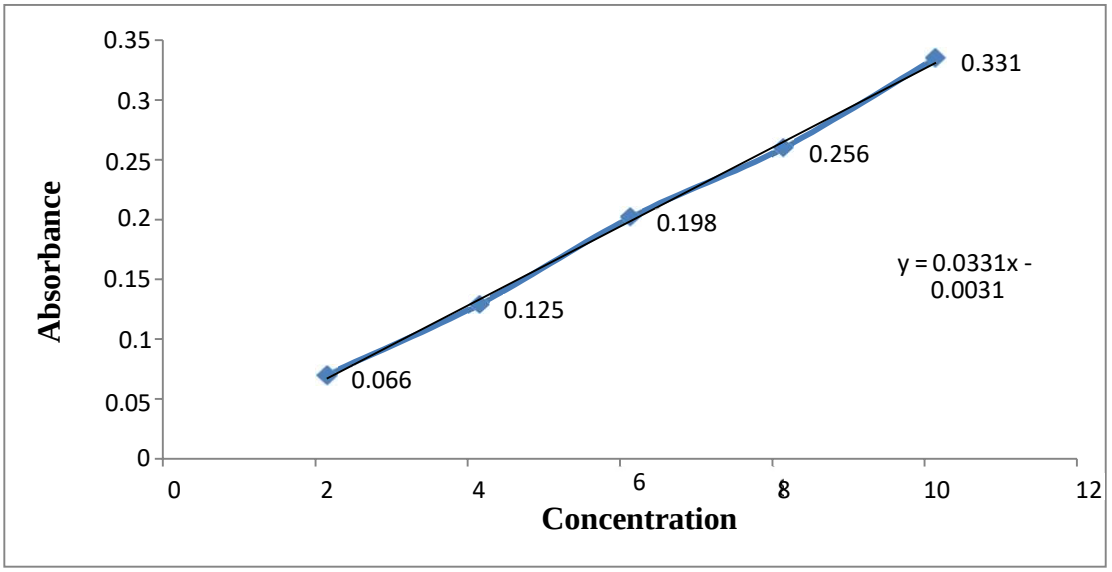



**Figure 5: Calibration curve of Cimetidine in distilled water**

**Table No. 6: Absorbance data of Cimetidine in phosphate buffer pH 6.8 for preparation of calibration curve, at 237.80 nm.**

| S. No. | Concentration (µg/ml) | Absorbance (n=3) |
|---|---|---|
| 1 | 2 | 0.145±0.6 |
| 2 | 4 | 0.296±0.2 |
| 3 | 6 | 0.443±0.7 |
| 4 | 8 | 0.641±0.2 |
| 5 | 10 | 0.765±0.1 |

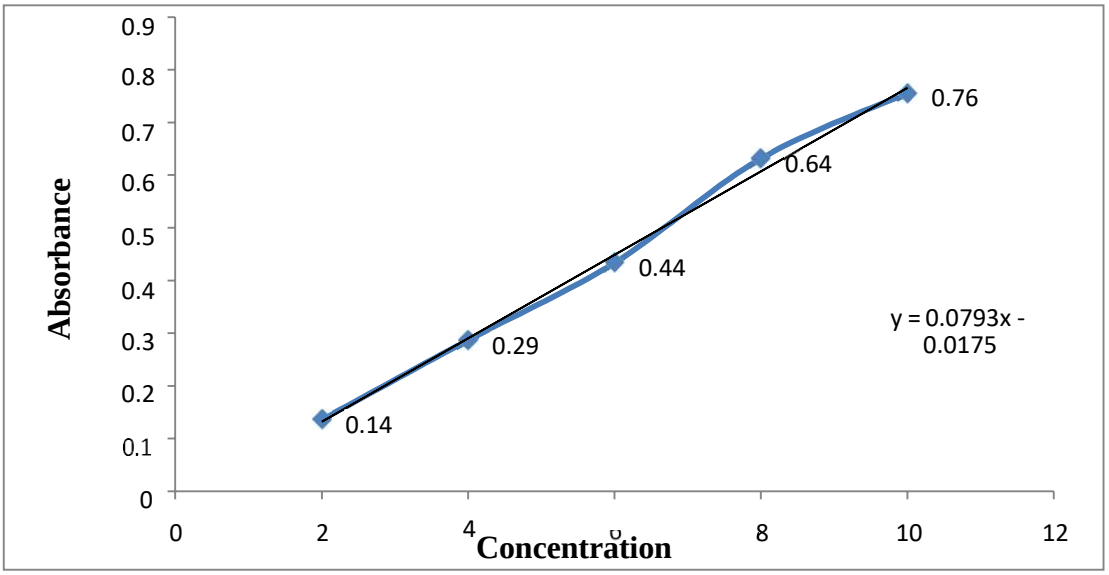



**Figure 6: Calibration curve of Cimetidine in Phosphate Buffer pH 6.8**

- **Determination of solubility of Cimetidine in various medium:** The solubility of Cimetidine in various mediums was studied and the results of study were shown in below table no.8.

**Table No. 7: Solubility study data of Cimetidine in different mediums:**

| S.No. | Solvent | Solubility of Cimetidine (µg/ml) |
|---|---|---|
| 1 | Distilled water | 4.06±0.11µg/ml |
| 2 | Phosphate buffer (pH) 6.8 | 574.19±0.12µg/ml |

- **Drug-excipient interaction study:** Cimetidine was shown to be compatible with a number of excipients that were chosen for the Fast-dissolving tablet formulation. The compatibility was assessed by TLC and the retention factors of all ratios were found similar.

**Table No. 8: Data of drug-excipient interaction study**

| S.No. | Drug/ drug+ Excipient Ratio (1:1) | Present Day (Rf) | Present 8 Days (Rf) | After 14 Days (Rf) |
|---|---|---|---|---|
| 1 | Drug (Cimetidine) | 0.531± 0.01 | 0.531±0. 01 | 0.531 ±0.02 |
| 2 | Drug + PVP-K 30 | 0.541± 0.86 | 0.541±0. 85 | 0.541 ±0.08 |

| | | | | |
|---|---|---|---|---|
| 3 | Drug + Fenugreek gum | 0.730± 0.81 | 0.730±0. 81 | 0.730 ±0.82 |
| 4 | Drug + Croscarmellose Sodium | 0.508± 0.89 | 0.508±0. 89 | 0.508 ±0.87 |
| 5 | Drug + Sodium Starch Glycolate | 0.510± 0.81 | 0.510±0. 80 | 0.510 ±0.81 |
| 6 | Drug + Micro Crystalline Cellulose | 0.566± 0.86 | 0.566±0. 86 | 0.566 ±0.89 |
| 7 | Drug + Mannitol | 0.616± 0.63 | 0.616±0. 61 | 0.616 ±0.61 |
| 8 | Drug + Magnesium Sterate | 0.583± 0.71 | 0.583±0. 71 | 0.583 ±0.72 |
| 9 | Drug + Talc | 0.591± 0.52 | 0.591±0. 50 | 0.591 ±0.55 |

- **Determination of various flow properties:**
- **Bulk density**, **tapped density**, **Carr's index**, **Hausner's ratio**, **Angle of repose:** The bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose of selected formulations were performed and shown in table no.-. All the results show that the final formulations possess a good flow property.

**Table No.9: Various flow properties of formulation F1– F9:**

| Characterization | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| **Bulk density (g/ml)** | 1.35± 0.23 | 1.33± 0.14 | 1.31± 0.21 | 1.36± 0.40 | 1.37± 0.41 \ | 1.39± 0.28 | 1.37± 0.26 | 1.37± 0.44 | 1.36± 0.08 |
| **Tapped density (g/ml)** | 1.58± 0.14 | 1.60± 0.24 | 1.62± 0.23 | 1.58± 0.08 | 1.58± 0.19 | 1.58± 0.22 | 1.56± 0.16 | 1.58± 0.20 | 1.58± 0.26 |
| **Carr's index (%)** | 14.55 | 16.87 | 19.13 | 13.92 | 13.29 | 12.02 | 12.17 | 13.29 | 13.92 |
| **Hausner's ratio** | 1.17 | 1.20 | 1.23 | 1.16 | 1.15 | 1.13 | 1.13 | 1.15 | 1.16 |
| **Angle of Repose ( $^0$)** | 26 $^0$ | 30 $^0$ | 25 $^0$ | 24 $^0$ | 29 $^0$ | 27 $^0$ | 28 $^0$ | 30 $^0$ | 29 $^0$ |

Data are represented as mean ±SD (n=3).

- **FORMULATION AND DEVELOPMENT:**

1. **Formulation of FDTs:**

   Fenugreek gum was used as an organic super disintegrant in the direct compression method used to create cimetidine FDTs. The formulations of Cimetidine and typical synthetic super disintegrants, such as SSG and Croscarmellose Sodium, were compared. The pills were prepared to be taken.

2. **Evaluation of Fast Dissolving Tablets:** The various physicochemical properties were evaluated like thickness, hardness, weight variation, friability, drug content, disintegration time, and wetting time and the study's findings are displayed in the table below:

**Table No 10: Weight Uniformity, Thickness, Hardness, and Percentage Friability of Batch F1-F9**

| Batch | Weight Variation Mean ± SD | Thickness Mean ± SD | Hardness ($Kg/cm^2$)(n=3) Mean±SD | Friability Mean ± SD |
|---|---|---|---|---|
| F1 | 350.0±0.81 | 3.99±0.2 | 2.6±0.264 | 0.845±0.01 |
| F2 | 350.1±0.26 | 3.98±0.1 | 2.4±0.173 | 0.704±0.01 |
| F3 | 350.1±0.39 | 3.99±0.2 | 3.0±0.057 | 0.561±0.02 |
| F4 | 348.4±0.89 | 3.98±0.01 | 2.9±0.152 | 0.702±0.1 |
| F5 | 348.6±0.93 | 3.98±0.02 | 3.0±0.1 | 0.571±0.02 |
| F6 | 350.1±0.32 | 3.99±0.6 | 3.0±0.057 | 0.568±0.01 |
| F7 | 350.1±0.29 | 3.98±0.2 | 3.0±0.057 | 0.842±0.02 |
| F8 | 349.1±0.43 | 3.99±0.2 | 3.1±0.1 | 0.560±0.02 |
| F9 | 349.6±0.28 | 3.98±0.2 | 3.1±0.057 | 0.835±0.01 |

**Table No. 11: Wetting time, Drug Content Uniformity, Water Absorption Ratio, Disintegration Time and In-vitro dissolution of Batch F1-F9.**

| Batch | Wetting Time (Sec) ± SD | (%) Drug Content Uniformity ± SD | Water Absorption Ratio (%) | Disintegration time (sec)±SD |
|---|---|---|---|---|
| F1 | 33±1 | 99.23±0.53 | 66.10±0.25 | 41±3 |
| F2 | 25±2 | 99.34±0.44 | 61.15±0.90 | 32±2 |
| F3 | 15±1 | 99.64±0.24 | 63.00±0.19 | 21±3 |
| F4 | 46±2 | 99.56±0.14 | 69.70±0.20 | 51±2 |
| F5 | 35±1 | 99.05±0.65 | 66.65±1.01 | 43±3 |
| F6 | 23±1 | 98.62±0.61 | 62.30±0.90 | 31±1 |
| F7 | 41±3 | 99.23±0.40 | 70.00±0.32 | 47±2 |
| F8 | 30±2 | 99.11±0.56 | 66.10±0.20 | 36±3 |
| F9 | 22±3 | 99.17±0.26 | 62.00±0.30 | 27±3 |

All value expressed in Standard deviation (n=3)

- **In-vitro drug release study for fast dissolving tablet:** The percentage drug release from formulations F1 to F9 was found to be more than 95% drug within 25 minutes.

**Table No. 12: Percentage drug release data of F1 to F9 formulation of Fast dissolving tablets.**

| S. No. | Time (in min) | % Drug Release data | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 1. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2. | 1 | 11.67± 0.56 | 12.44± 0.60 | 14.54± 0.80 | 12.95± 0.89 | 16.62± 0.53 | 15.01± 0.90 | 13.56± 0.92 | 14.55± 0.58 | 17.25± 0.20 |
| 3. | 2 | 22.25± 0.50 | 24.55± 0.58 | 27.01± 0.14 | 24.65± 0.53 | 20.08± 0.56 | 27.86± 0.60 | 22.45± 0.53 | 26.42± 0.80 | 27.91± 0.83 |
| 4. | 3 | 34.93± 1.30 | 36.42± 0.56 | 38.94± 0.58 | 36.82± 0.56 | 32.25± 0.80 | 30.21± 0.30 | 34.56± 1.40 | 37.14± 0.60 | 35.65± 0.82 |
| 5. | 5 | 45.55± 0.58 | 47.14± 0.56 | 50.57± 0.59 | 47.91± 1.20 | 44.56± 0.80 | 42.54± 0.56 | 47.95± 0.72 | 49.95± 0.80 | 50.15± 0.56 |
| 6. | 10 | 67.5± 0.50 | 69.95± 0.63 | 72.98± 0.53 | 59.98± 0.32 | 67.98± 0.78 | 54.99± 0.40 | 59.78± 0.54 | 54.17± 0.80 | 66.45± 0.60 |
| 7. | 15 | 72.45± 0.60 | 74.17± 0.63 | 82.52± 0.40 | 71.54± 0.56 | 79.78± 1.56 | 76.98± 0.76 | 66.66± 0.56 | 73.02± 0.20 | 81.26± 0.56 |
| 8. | 20 | 79.45± 2.30 | 83.02± 1.20 | 88.24± 0.30 | 79.56± 0.58 | 86.56± 0.30 | 89.84± 0.45 | 75.84± 0.73 | 86.23± 0.23 | 86.21± 0.60 |
| 9. | 25 | 81.21± 1.20 | 90.23± 0.40 | 98.05± 0.45 | 85.23± 0.40 | 90.34± 0.12 | 93.29± 0.50 | 86.01± 036 | 91.01± 0.63 | 94.54± 0.56 |

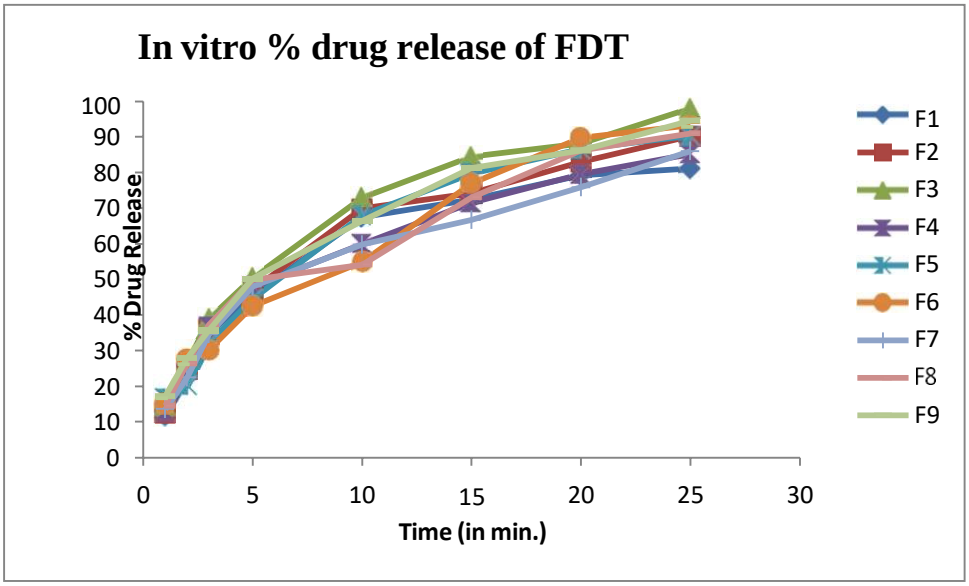



**Figure 7: Percentage Drug Release from Fast dissolving tablets Formulation.**

- **Stability studies:** In the stability chamber, the stability investigations F-3 Formulation were conducted for a duration of one month. The tablets were kept at the 400C±20C and 75±5%RH, Q1C, temperatures suggested by the ICH recommendations. Every 30 days, the tablets were taken out and examined for changes in weight, hardness, disintegration, wetting time, drug content, etc. Table No. 12 presents the results.

**Table No. 13 Stability study for fast dissolving tablet of Formulation batch (F-3).**

| S.No. | Parameter | 0 days | 15 days | 30 days | Result |
|---|---|---|---|---|---|
| 1. | Weight Uniformity | 350.1±0.32 | 350.1±0.39 | 350.1±0.41 | No change |
| 2. | Hardness | 4.0±0.25 | 4.0±0.16 | 4.0±0.15 | No change |
| 3. | Drug content | 99.64±0.34 | 99.64±0.24 | 99.62±0.22 | Some change |
| 4. | Wetting time | 15±12 | 15±11 | 15±17 | No change |
| 5. | Disintegration | 21±43 | 21±02 | 21±08 | No change |

## ➢ SUMMARY AND CONCLUSION:

The objective of this work was to use fenugreek gum, a natural super disintegrant, to create a fast-acting cimetidine drug delivery system. The goal of this study was to create medicine delivery tablets that dissolve quickly and assess if fenugreek gum may speed up the pace at which cimetidine dissolves. Drug release characteristics of nine distinct formulations (designated F1 through F9) were examined over a quarter of an hour.

To ascertain the fenugreek gum's qualities and appropriateness as a super disintegrant, it was first extracted and put through a physicochemical examination. Drug release from the formulations was measured at predetermined intervals. All formulations exhibited no drug release during the first 2-minute interval; however, at the second 2-minute interval, the percentage of drug release varied, ranging from 11.67% for F1 to 17.25% for F9. The measurements' standard deviation was comparatively low, suggesting uniformity among the formulas. The percentage of medication release rose dramatically over time. F1 released 81.21% of the drug by the 25-minute mark, which was determined to be the peak drug release time, whereas F9 released 94.54%. All formulations were effective in rapidly releasing the drug, but F3 stood out as the most efficient.

The study proved that fenugreek gum works well as a natural super disintegrant when it comes to making fast-acting cimetidine pills. The physicochemical examination of fenugreek gum verified its appropriateness for this particular use. All nine of the studied formulations demonstrated measurable drug release in a short amount of time, with formulation F3 demonstrating the highest level of efficiency. The tiny standard deviations, which show consistency in the drug release percentages, imply that the formulations are dependable and repeatable.

With a maximum drug release of 98 % at 25 minutes, F3 performs better than the other evaluated formulations, indicating that it has the most effective drug release profile. The study offers a viable method for using fenugreek gum to increase the pace at which cimetidine dissolves. Particularly the formulation F3 shows promise for quick and effective drug administration, which makes it a solid contender for more research and possible clinical use. This study adds to the continuing attempts to use natural and biocompatible materials to improve medication delivery systems' performance.

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