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## **FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF METFORMIN**

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### **ABSTRACT**

Objective of this study was to formulate directly compressible fast dissolving tablets of Metformin with sufficient mechanical integrity, content uniformity, and acceptable palatability to assist patients of any age group for easy administration. Effect of varying concentrations of different synthetic superdisintegrants such as croscopolone, croscarmellose sodium, and natural superdisintegrants such as *Plantago ovata* and *Fenugreek* on disintegration time was studied. Tablets were evaluated for weight variation, thickness, hardness, friability, taste, drug content, in vitro disintegrating time and in vitro drug release. Other parameters such as wetting time, water absorption ratio were also evaluated. The disintegration time of the optimized F6 was found to be  $24.5 \pm 1.04$  secs.

## INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, Pain avoidance and most importantly the patient compliance. The most popular solid Dosage forms being the tablets and capsules; one important drawback of this dosage forms for some patients, is difficulty in swallowing. Drinking water plays an important role in the Swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Dispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people.

Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapi-melts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics. Their growing importance was underlined recently when European pharmacopoeia adopted the term "or dispersible tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach in development of FDT is the use of super disintegrants like cross linked carboxymethylcellulose (Crosscarmellose), sodium starch glycolate (primo gel, explotab), polyvinylpyrrolidone, Polyplasdone) etc., which provide instantaneous disintegration of tablet after putting on tongue, thereby it release the drug in saliva.

## EVALUATION PARAMETERS TO BE STUDIED FOR FAST DISSOLVING TABLETS

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. The various evaluation testing includes tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

- **Size and Shape**

The size and shape of the tablet can be dimensionally described, monitored and controlled.

- **Weight variation:**

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

- **Drug Content Estimation**

Ten tablets were taken and amount of drug present in each tablet was determined as follows: Tablet was crushed in mortar and transferred to 100 ml flask. The powder was dissolved in pH 3.2. The sample was mixed by using Remi mixer for 5 minutes, after which it was filtered through Whatman filter paper. The filtered solutions after appropriate dilution (1 to 10 ml) with 0.1 N HCL were analyzed by validated UV Spectrophotometric method at  $\lambda_{\text{max}}$  283nm.

- **Mechanical Strength**

Tablets should possess adequate strength to withstand mechanical shocks of handling in manufacturing, packaging and shipping. Crushing strength and friability are two important parameters to evaluate the tablet for its mechanical strength.

- **Crushing Strength**

It is the force required to break a tablet by compression in the radial direction, it is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. In the present study the crushing strength of the tablet was measured using Pfizer hardness testers. An average of three observations is reported.

- **Friability test (F)**

The crushing test may not be the best measure of potential behavior during handling and packaging. The resistance to surface abrasion may be a more relevant parameter. Friability of each batch was measure in “Electro lab friabilator”. Ten pre weighed tablets were rotated at 25 rpm for 4 min, the tablets were then re weighed and the percentage of weight loss was calculated. The friability (F) is given by the formula.

$$F = (W_{\text{initial}} - W_{\text{final}}) / W_{\text{initial}} \times 100$$

- **Wetting time and Water Absorption Ratio:**

Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper

surface of the tablet is noted as a wetting time. The wetted tablet was then weighed and the water absorption ratio, R, was determined according to equation:

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

Where,

$W_b$  and  $W_a$  are the weights of tablet before and after water absorption, respectively.

- ***In vitro* dispersion time**

*In vitro* dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Three tablets from each formulation were randomly selected and *in vitro* dispersion time was performed.

- ***In vitro* disintegration time**

*In vitro* disintegration time was performed by apparatus specified in USP at 50rpm. Phosphate buffer pH-6.8, 900 ml was used as disintegration medium, and the temperature of which maintained at  $37 \pm 2^\circ\text{C}$  and the time in second taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

## **MATERIALS AND METHODS**

Metformin was procured by Wockhardt Pharma., Baddi, Crosscarmellose sodium, Sodium starch glycolate, are gifted by Signet chemical corporation, Mumbai.

### **FORMULATION OF FAST DISSOLVING TABLETS OF METFORMIN**

As shown in Table 1 and 2 Fast dissolving tablets containing 200 mg of Metformin were prepared by direct compression method and the various formulae used in the study are shown in. The drug and excipients were passed through sieve (#80) to ensure better mixing. Synthetic Superdisintegrants like Crospovidone, Croscarmellose sodium and natural Superdisintegrants *Plantago ovate* and *fenugreek* powders were used in 4% and 8% concentration. All the ingredients were mixed uniformly followed by addition of magnesium stearate and talc. Tablets were compressed using 8 mm punch using RIMEK 8 station tablet compression machine.

#### **Preparation of seed powder of *Plantago ovata*:**

The dried *Plantago ovata* seeds were comminuted and sieved through mesh no. 80 and stored in desiccator.

#### **Preparation of seed powder of *Fenugreek*:**

The dried *Fenugreek* seeds were comminuted and sieved through mesh no. 80 and stored in desiccator.

**TABLE 1- FORMULATION OF METFORMIN FAST DISSOLVING TABLETS**

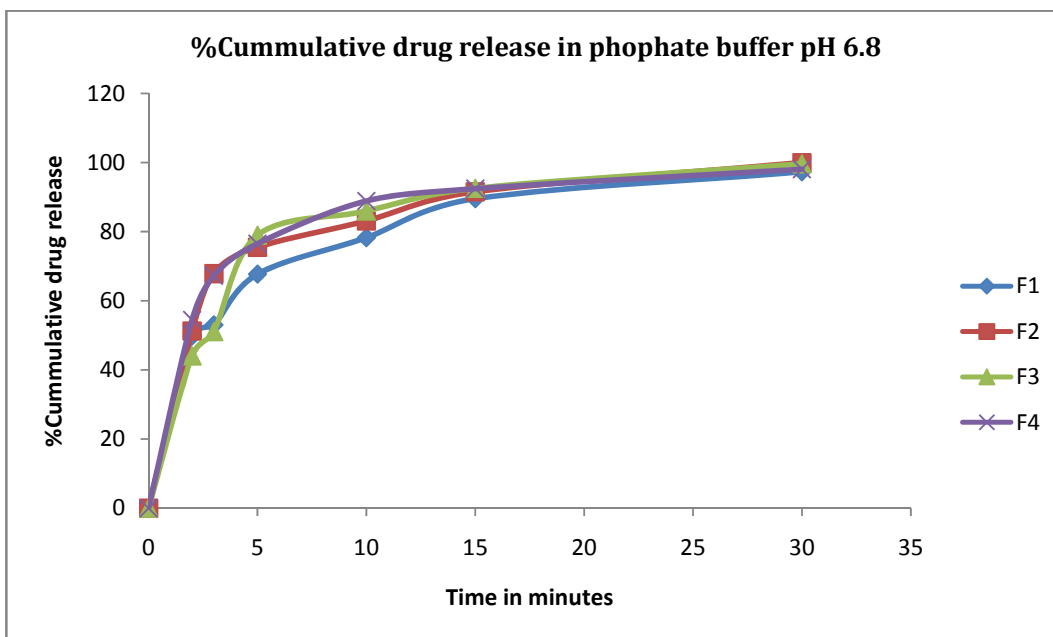
| Sl.No.       | Ingredients Name       | F <sub>1</sub><br>(mg) | F <sub>2</sub><br>(mg) | F <sub>3</sub><br>(mg) | F <sub>4</sub><br>(mg) | F <sub>5</sub><br>(mg) | F <sub>6</sub><br>(mg) | F <sub>7</sub><br>(mg) | F <sub>8</sub><br>(mg) |
|--------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| 1.           | Metformin              | 100                    | 100                    | 100                    | 100                    | 100                    | 100                    | 100                    | 100                    |
| 2.           | Crosscarmellose Sodium | 8                      | 16                     | -                      | -                      | -                      | -                      | -                      | -                      |
| 3.           | Crosspovidone          | -                      | -                      | 8                      | 16                     | -                      | -                      | -                      | -                      |
| 4.           | Isaphagula             | -                      | -                      | -                      | -                      | 8                      | 16                     | -                      | -                      |
| 5.           | Fenugreek              | -                      | -                      | -                      | -                      | -                      | -                      | 8                      | 16                     |
| 6.           | Lactose                | 32                     | 24                     | 32                     | 24                     | 32                     | 24                     | 32                     | 24                     |
| 7.           | Mannitol               | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     |
| 8.           | Magnesium Stearate     | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     |
| 9.           | Talc                   | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     | 20                     |
| Total weight |                        | 200                    | 200                    | 200                    | 200                    | 200                    | 200                    | 200                    | 200                    |

**TABLE 2- EVALUATION PARAMETERS FOR METFORMIN FAST DISSOLVING TABLETS**

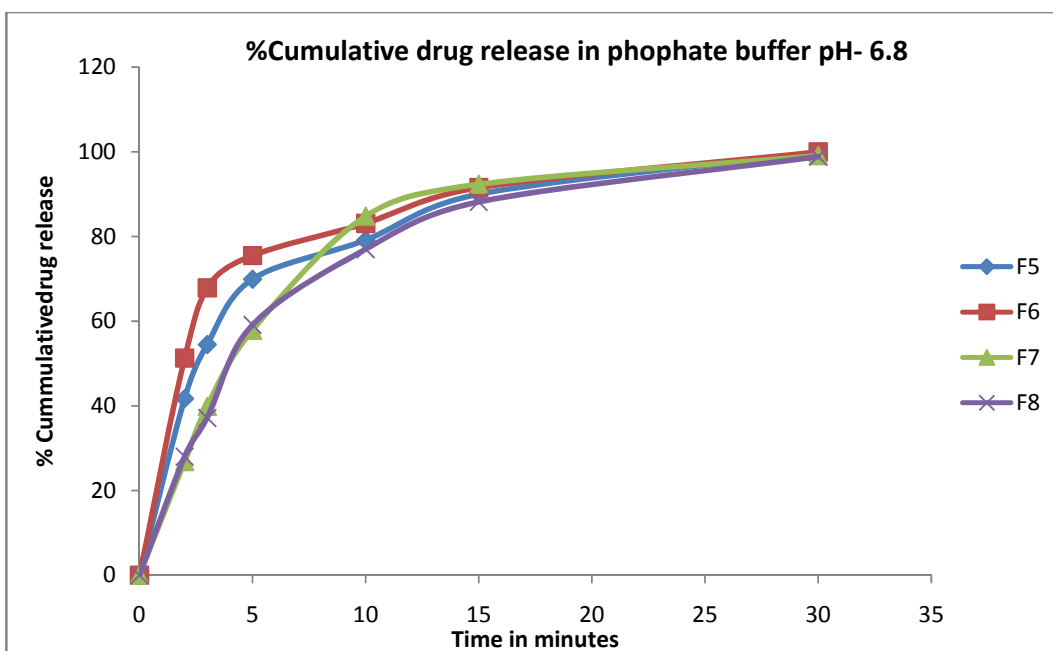
| Parameters | Hardness<br>(kg/cm <sup>2</sup> ) | DT (secs) | Friability<br>(%) | Wetting<br>time (secs) | Dispersion<br>time (secs) | Drug<br>content (%) | Weight<br>variation (%) |
|------------|-----------------------------------|-----------|-------------------|------------------------|---------------------------|---------------------|-------------------------|
| <b>F1</b>  | 4.5±0.08                          | 61.5±0.54 | 0.65±0.01         | 60.1±1.16              | 43.6±0.81                 | 99.6±0.8            | 99.8±1.1                |
| <b>F2</b>  | 4.4±0.07                          | 54.5±1.04 | 0.61±0.01         | 44.8±1.16              | 37.5±1.04                 | 99.8±0.9            | 99.5±1.04               |
| <b>F3</b>  | 4.41±0.1                          | 47.1±0.75 | 0.57±0.008        | 38.1±1.4               | 32.8±1.1                  | 99.1±1.1            | 99.3±1.3                |
| <b>F4</b>  | 4.2±0.08                          | 40.3±1.03 | 0.52±0.012        | 33.6±1.2               | 28.1±0.7                  | 100.3±1.0           | 100.3±0.8               |
| <b>F5</b>  | 4.1±0.09                          | 30.8±1.16 | 0.47±0.01         | 25.6±1.03              | 23.5±0.54                 | 100.6±0.5           | 101.1±0.7               |
| <b>F6</b>  | 3.7±0.10                          | 24.5±1.04 | 0.44±0.01         | 17.1±0.75              | 16.3±0.8                  | 100±1.2             | 100.5±1.0               |
| <b>F7</b>  | 3.08±0.1                          | 60.8±0.7  | 0.63±0.008        | 59.1±0.7               | 42.6±0.5                  | 99.6±0.5            | 100.3±0.8               |
| <b>F8</b>  | 2.8±0.1                           | 53.6±0.8  | 0.60±0.005        | 44.5±1.04              | 36.1±0.7                  | 100±0.8             | 99.6±0.8                |

**TABLE 3 - *IN-VITRO* DRUG RELEASE STUDY OF METFORMIN FAST DISSOLVING TABLETS**

| Time in<br>minutes | F1    | F2    | F3    | F4    | F5    | F6    | F7    | F8    |
|--------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| <b>0</b>           | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
| <b>2</b>           | 49.83 | 51.28 | 44.04 | 54.47 | 41.72 | 51.28 | 26.83 | 27.98 |
| <b>3</b>           | 53.02 | 67.87 | 51.08 | 67.23 | 54.47 | 67.87 | 39.89 | 37.13 |
| <b>5</b>           | 67.72 | 75.49 | 78.98 | 76.51 | 69.90 | 75.49 | 57.87 | 59.11 |
| <b>10</b>          | 78.25 | 83.09 | 85.98 | 88.88 | 79.12 | 83.09 | 84.81 | 76.98 |
| <b>15</b>          | 89.54 | 91.54 | 92.54 | 92.43 | 89.99 | 91.54 | 92.32 | 88.17 |
| <b>30</b>          | 97.32 | 99.97 | 99.65 | 98.06 | 99.89 | 99.97 | 99.08 | 98.87 |



a. Cumulative % drug release of the Metformin FDTs for the formulation F1, F2, F3, F4.



b. Cumulative % drug release of the Metformin FDTs for the formulation F5, F6, F7, F8.

**Figure 1- *In-vitro* cumulative drug release for Metformin Fast Dissolving tablets using phosphate buffer P<sup>H</sup> 6.8**

## RESULTS AND DISCUSSION

Fast dissolving tablets of Metformin was formulated by using the superdisintegrants (Crospovidone, Croscarmellose, *Plantago ovata* and *Fenugreek*) by taking 4% and 8% each. The prepared FDTs were subjected to various evaluation tests.

All the formulations had passed the pre-formulation characteristics showing good flow property. Hardness for the formulations F1 – F8 was found to be in the range of  $4.5 \pm 0.08$  to  $2.8 \pm 0.1$  Kg/cm<sup>2</sup>, DT was found to be in the range of  $61.5 \pm 0.54$  to  $53.6 \pm 0.8$  secs, Friability and weight variation was seen to pass the requirements. It was observed very clearly that with the increasing concentration of superdisintegrants the hardness and disintegration decreased. Out of all the eight formulations F6 showed the best features with least DT of  $24.5 \pm 1.04$  seconds. This is due to the effect of natural superdisintegrants and the mechanism acting behind. The in vitro drug release was studied for all the formulations and the drug release ranged from 97.32 to 99.97 % respectively. The evaluation parameters showed that the use of natural superdisintegrants showed better hardness and DT w.r.t wetting time and drug release as compared to synthetic superdisintegrants.

## CONCLUSION

From the above results done it is concluded that formulation F6 shows better result with proper Hardness of  $3.7 \pm 0.10$  kg/cm<sup>2</sup>, DT of  $24.5 \pm 1.04$  secs,  $0.44 \pm 0.01\%$  Friability, Wetting time  $17.1 \pm 0.75$  secs, Dispersion time  $16.3 \pm 0.8$  secs having Drug content  $100 \pm 1.2\%$ . It fulfils all the requirements for a Fast Dissolving Tablet. This formulation shows maximum Drug release of 99.97%. Formulation F6 is found to be better due to less DT and wetting time with proper hardness as compared to other formulations consisting of synthetic and natural superdisintegrants. So it is concluded that the use of natural superdisintegrants in comparison to synthetic superdisintegrants is better in terms of hardness, DT and it is economical too.

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