**To Formulation and Evaluation Fast dissolving tablet of Glipizide.**

Aditya Ashok Bahir ,Prof.Nandini A .Patil, Dr.Megha T. Salve

 Shivajirao pawar college of pharmacy, Pachegaon Tal- Newasa

 Dist-Ahilyanagar – 413725

**Abstract**

Aim of the present study was to develop the Fast-Dissolving Oral flicks of Glipizide. It's alternate- generation sulfonylurea that can acutely lower the blood glucose position. Fast dissolving oral flicks deliver medicine directly in the vascular system and bypasses the hepatic first pass metabolism so cure of the medicine may also reduce significantly. Fast dissolving flicks were prepared using solvent casting system, hydrophilic polymers (HPMC K- 15, HPMCE-15, HPMC K- 100) were named as film forming agents and cut- 400 was used as plasticizer to give inflexibility to the flicks. In FT- IR study no commerce was observed between medicine and the excipients. Three blank flicks were named for the objectification of medicine. After characterization the medicine loaded flicks and studying their decomposition time & in- vitr medicine release studies, among them was named the stylish expression as its decomposition and dissolution time was less and it releases medicine to a lesser extent from 93 to further than 100 in ten twinkles. expression was named stylish expression as its decomposition and dissolution time was less and it released medicine to a lesser extent compared to other phrasings. thus, presto dissolving oral flicks can play an important part in oral medicine delivery. Drug loaded flicks with both the polymers were stable under 40 °C/ 75 RH conditions.

**Keywords:** Fast Dissolving Tablets, Glipizide, HPMC, Solvent casting method, Drug release.

# **INTRODUCTION**

* **Fast Dissolving Tablets (FDTs)**

Fast dissolving tablets, in general, are defined as solid oral lozenge forms that disintegrate and dissolve in mouth without water within 60 seconds or lower (Pfister and Gosh, 2005). According to FDA's Center for medicine Evaluation and exploration (CDER), fast dissolving tablets are defined as" A solid lozenge form containing medicinal substances, which disintegrates fleetly generally within a matter of seconds, when placed on the lingo"(FDA- Guidance for assiduity, 2007). The growing significance of fast dissolving lozenge forms is honored by assiduity as well as academia. The global trade for fast dissolving tablets was estimated at$ 2.4 billion in 2004 and$ 3 billion in 2006 (Van Arnum, 2006). Grounded on different technologies more than 50 marketable products are available in the request. These products can deliver medicines like desloratadine (antihistamine), piroxicam (NSAID), risperidone (antipsychotic), rizatriptan (antimigraine), famotidine(anti-ulcer), ondansetron (antiemetic), selegiline (antiparkinson) and roxithromycin (antibiotic). This growing significance was underscored lately when European Pharmacopoeia espoused the term orodispersible tablet and before this time FDA, issued draft guidance, Guidance for assiduity Orally Disintegrating Tablets. According to European Pharmacopoeia, orodispersible tablet is" a tablet which disperses and disintegrates in lower than 3 twinkles in the mouth before swallowing". The draft guidance issue lately by the FDA recommended, in addition to the original description, orally disintegrating tablets be considered solid oral medications that disintegrate fleetly in the oral depression with an in vitro decomposition time of roughly 30 seconds or lower, when grounded on the United States Pharmacopoeia decomposition test system or volition (FDA- Guidance for assiduity, 2007). FDTs release medicine in the mouth for immersion through original oromucosal apkins and through pregastric (eg. oral depression, pharynx, and esophagus), gastric (i.e.stomach), and postgastric (eg.small and large bowel) parts of the gastrointestinal tract (Pfister and Gosh, 2005).

* **Advantages of Fast Dissolving Tablets**

The advantages of fast dissolving tablets are as follows

1. Ease of administration to pediatric, senior and psychiatric cases. Accessible administration to cases who cannot swallow, similar as the mentally ill, impaired and uncooperative, stroke victims, healthcare installation and bedridden cases.
2. It allows ease of termination of remedy.
3. It gives rapid-fire dissolution of the medicine and immersion, which may produce rapid-fire onset of action. Some medicines may get absorbed from the mouth, pharynx and esophagus as the slaver passes down the stomach. This pregastric immersion may give bettered bioavailability. Pregastric immersion may also reduce the cure of the medicine if a significant quantum of the medicine is lost through hepatic metabolism. As a result of reduced lozenge, it may give bettered clinical performance and reduction of unwanted goods.
4. It has all the advantages of solid lozenge forms, which include better stability, accurate dosing, easy manufacturing, small pack size and ease of running of cases.
5. The largely salutary point of this lozenge form is the cases who are traveling and busy people who do n't have immediate access to water can swallow this lozenge form veritably fluently.
6. These lozenge forms have the capability to give the advantages of liquid drug in the form of solid medication. These advantages include easy administration and free of the threat of suffocation performing from physical inhibition by a lozenge form.
7. Fast dissolving tablets are considered as a new lozenge form. thus, pharmaceutical companies may get different advantages similar as line extension and life cycle operation, patent life extension, exclusivity of product creation and product isolation.
* **Desirable characteristics and experimental challenges of FDTs.**

The desirable characteristics of FDTs are described below

* **Fast Decomposition**

FDTs should disintegrate in the mouth without fresh water or with a veritably small quantum of water. The decomposition fluid is handed by the slaver of the case. The disintegrated tablet should come a soft paste or liquid suspense, which can give a good mouth feel and smooth swallowing. The “fast decomposition” generally means decomposition of tablets in lower than 1 nanosecond, but it's preferred to have decomposition as soon as possible.

* **Taste of Active constituents**

Because FDTs dissolve or disintegrate in the case’s mouth, the medicine will be incompletely dissolved in close propinquity to the taste kids. After swallowing, there should be minimum or no residue in the mouth.

* **Drug Properties**

For the ideal FDT technology, the medicine parcels should n't significantly affect the tablet property. numerous medicine parcels could potentially affect the performance of FDTs. For illustration, the solubility, demitasse morphology, flyspeck size, hygroscopicity, compressibility, and bulk viscosity of a medicine can significantly affect the final tablet’s characteristics, similar as tablet strength and decomposition.

* **Tablet Strength and Porosity**

Because FDTs are designed to have a quick dissolution/ decomposition time, the tablet porosity is generally maximized to insure fast water immersion into the tablets. The crucial parcels of the tablets are fast immersion or wetting of water into the tablets and the decomposition of associated patches into individual factors for fast dissolution. This requires that excipients should have high wettability, and the tablet structure should also have a largely pervious network.

* **Humidity perceptivity**

 FDTs should have low perceptivity to moisture. This problem can be especially grueling because numerous largely water-answerable excipients are used in expression to enhance fast dissolving parcels as well as to produce good mouth feel.

* **Materials And Methods**

Glipizide, Soluble starch, Talc, Magnesium stearate, Microcrystalline cellulose, Maize starch

### **Preparation of Fast Dissolving Tablets**

Screened materials passed through a no. 100 screens were selected as superdisintegrants. Glipizide, microcrystalline cellulose, superdisintegrant and soluble starch were weighed and mixed together for 5 min in a resealable plastic bag. The powder blends were lubricated with talc and magnesium stearate to make flow property excellent. The powder blends ready for compression were transformed into tablets using a tablet punching machine (Cadmach, India) at a compression force of 3.5 tons.

* **Formulation composition of Glipizide**

**Table: Formulation composition of Glipizide**

|  |  |  |
| --- | --- | --- |
| **Ingredients (%)**  | **Formulation code** |  |
| TPOH 1  | TPOH 2  |  TPOH 3  | TPOH 4  | TPOH 5  | TPOH 6  | TPOH 7  |
| Glipizide | 2  | 2  | 2  | 2  | 2  | 2  | 2  |
| TPOH  | 1  | 3  | 5  | 7  | 9  | 12  | 15  |
| MCC  | 35  | 35  | 35  | 35  | 35  | 35  | 35  |
| Talc  | 1  | 1  | 1  | 1  | 1  | 1  | 1  |
| Magnesium stearate  | 1  | 1  | 1  | 1  | 1  | 1  | 1  |
| Starch soluble q.s. (mg)  | 250  | 250  | 250  | 250  | 250  | 250  | 250  |

### **Evaluation of Fast Dissolving Tablets**

#### **Drug Content Study**

A aimlessly named tablet was crushed in a glass mortar and pestle, and the powdered tablet was suspended in 100 mL of phosphate buffer (pH 7.4) with shifting on a glamorous stirrer. After 24 hours, the result was filtered and the filtrate was anatomized by UV- 1800 spectrophotometer (Shimadzu, Japan) at 225 nm. The medicine content was calculated using the formula;

Drug content = [Practical drug content/ Theoretical drug content] ×100.

#### **Content Uniformity Study**

For the content uniformity assessment, random samples of 10 tablets were labeled without any specific order and analyzed together using a UV-1800 spectrophotometer (Shimadzu, Japan) at 225 nm. The required specification for this examination is that the consistency of the lozenge units must fall between 85 and 115, with a relative standard deviation of less than or equal to 6.

* **Hardness & Friability Study**

For the hardness test, 6 tablets were randomly chosen from every batch. The hardness test was conducted using a Monsanto hardness tester (Cadmach, Ahmedabad, India). The friability test was conducted utilizing a Roche friabilator (Campbell Electronics, Mumbai, India). A sample of 20 tablets randomly chosen from each batch was tested simultaneously. Following 100 turns, the tablet samples were assessed by measuring their weight.

#### **Disintegration Study**

The study on in vitro disintegration time for fast dissolving tablets was conducted using a modified disintegration test apparatus with distilled water, 0.1 M HCL, and phosphate buffer (pH 7.4) serving as the disintegrating medium (Khan et al., 2007). A more appropriate device was created due to numerous studies (Morita et al., 2000; Watanabe et al., 2004; Narazaki et al., 2004; Watanabe et al., 2001) highlighting the inadequacy of the traditional disintegration test equipment for fast-dissolving tablets. In summary, the setup included a 1000 ml glass beaker with a wire basket held in place by a support, so that when the beaker held 900 mL of the disintegrating medium, the tablet in the basket was fully submerged. A magnetic bead was positioned at the base of the beaker held at 37 ± 20C. Disintegration time was assessed at 25 rpm.

#### **Wetting Time Study**

The wetting time analysis of each tablet was conducted in distilled water, 0.1 M HCL, and phosphate buffer (pH 7.4) utilizing the method described by Bi et al with minor adjustments. A sheet of tissue paper folded twice was placed in a culture dish with 10 ml of distilled water (which also contained 0.1 M HCl and phosphate buffer at pH 7.4). A tablet with a small amount of amaranth powder on its top surface was set on the tissue paper. The duration needed for a red hue to appear on the tablet's upper surface was noted as the wetting time.

#### **Swelling Study**

The swelling assessment of the tablet was performed in swelling media like distilled water, 0.1 M HCL, and phosphate buffer (pH 7.4). In the swelling study, the tablet's initial weight was measured (W1). Subsequently, each tablet was individually placed in a 25-mL beaker filled with tissue paper saturated with swelling solution. Tablets were taken out after 2 minutes, cleaned with filter paper, and remeasured (W2). The swelling index was determined using the following method.

Swelling index = [(W2–W1) / W1] 100

#### **In vitro Dissolution Study**

In the FDT formulation, the assessment of glipizide release was conducted following the method outlined in the USP monograph (USP, 2011). The test was conducted using paddles rotating at 50 rpm, and the dissolution medium was made up of 900mL of phosphate buffer at pH 7.4 and 0.1 M HCl kept at a temperature of 37°C. A volume of two milliliters of dissolution medium was taken at 0.25, 0.5, 0.75, 1, 1.5, 2, and 2.5 hours, filtered with a membrane filter, and examined using a UV-1800 spectrophotometer (Shimadzu, Japan). New medium was exchanged following sample removal. For the commercially available formulation, the dissolution device and medium resembled those of the FDTs.

### **Differential Scanning Calorimetric (DSC) Analysis**

The DSC evaluation of pure glipizide and its physical mixture with excipient (1:1) was performed using DSC No 7 (Perkin Elmer) to assess any potential interactions between the drug and polymer. Samples were analyzed from 40 to 4000 C at a heating rate of 100 C min-1 while under a nitrogen purge with an approximate flow rate of 50 ml min-1. Samples (2-6 mg) were measured and securely sealed in standard aluminum containers.

* **Result and Discussion**

## **Standard Calibration Curve of Glipizide**

To acquire λ, the UV scan range was set between the wavelengths of 200-400 nm. It provided maximum peaks at 225 (highest) and 276 nm, as illustrated in the figure, and consequently, λmax 225 nm was chosen for measuring glipizide concentration. The standard calibration curve for glipizide was created by graphing absorbance against concentration. The calibration curve's linear regression equation was derived.

**Fig: Absorption maxima of glipizide in phosphate buffer (pH 7.4)**

**Fig: Standard curve of glipizide in phosphate buffer (pH 7.4) at λ 225 nm max**

Standard curve of glipizide

y = 0.0234x + 0.0031

R

2

 = 0.9993

0

0.5

1

0

5

10

15

20

25

30

35

40

45

**Conc (microgram/ml)**

**Absorbance**

The hardness of the formulations varied from 4.06 ± 0.23 to 8.56 ± 0.25 Kg. The formulation with 1% of TPOH exhibited the highest hardness. Illustrated the impact of TPOH concentration on the hardness of the tablets. A negligible relationship (p>0.05), showing negative correlation (R2=0.9812), was observed between TPOH concentration and tablet hardness, suggesting that an increase in TPOH concentration led to a decrease in tablet hardness.

# **Table: Evaluation Table for Drug Content Analysis and Content Uniformity**

|  |  |  |  |
| --- | --- | --- | --- |
| Sr. no. | Formulation code | Drug content (%)(n=3, ± SD) | Content Uniformity (%)(n=10, ± SD) |
| 1 | TPOH1 | 100.62 ± 1.77 | 99.23 ± 1.83 |
| 2 | TPOH2 | 99.19 ± 2.61 | 100.31 ± 1.93 |
| 3 | TPOH3 | 99.87 ± 1.41 | 99.23 ± 2.23 |
| 4 | TPOH4 | 99.62 ± 0.98 | 99.48 ± 1.22 |
| 5 | TPOH5 | 99.33 ± 1.70 | 100.40 ± 1.57 |
| 6 | TPOH6 | 100.31 ± 0.74 | 99.97 ± 1.58 |
| 7 | TPOH7 | 100.13 ± 0.77 | 99.23 ± 1.32 |

# **Table: Evaluation Table for Hardness, Friability (%) and Disintegration Time**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Sr. no. | Formulation code | Hardness (Kg) (n=6, ± SD) | Friability (%)(n=3, ± SD) | Disintegration time(sec) (n=3, ± SD) |
| 1 | TPOH1 | 8.56 ± 0.25 | 0 | 84.33 ± 4.35 |
| 2 | TPOH2 | 8.33 ± 0.11 | 0.03 ± 0.03 | 75.99 ± 3.51 |
| 3 | TPOH3 | 7.96 ± 0.25 | 0.04 ± 0.01 | 62.32 ± 3.78 |
| 4 | TPOH4 | 6.56 ± 0.11 | 0.06 ± 0.01 | 56.66 ± 2.51 |
| 5 | TPOH5 | 6.30 ± 0.43 | 0.14 ± 0.04 | 51.32 ± 2.08 |
| 6 | TPOH6 | 5.66 ± 0.30 | 0.26 ± 0.03 | 44.33 ± 3.60 |
| 7 | TPOH7 | 4.06 ± 0.23 | 0.31 ± 0.03 | 32.99 ± 2.51 |
|  |  | P>0.05, NS R2= - 0.9812 | P=0.008, S R2= 0.9688 | P=0.0001, HSR2= - 0.9854 |

As the concentration of TPOH rose from 1 % to 15 % w/w, the percentage of friability grew from 0 % to 0.14 %. In this study, the friability percentage for all formulations was under 1%, showing that it is within the allowed limits.

0.01

0.1

1

10

100

1

2

3

4

5

6

7

Conentration of TPOH (%)

Friability (%)

**Figure: Effect of TPOH concentration on percentage friability**

The formulation with 1% TPOH exhibited a very high wetting time, while the formulation with 15% TPOH showed the lowest wetting time. Comparable results were observed when the wetting test was conducted in 0.1 M HCL and phosphate buffer at pH 7.4. The influence of TPOH concentration on the duration of wetting.

1

10

100

1000

1

2

3

4

5

6

7

Concentration of TPOH (%)

Wetting time (sec)

**Figure: Effect of TPOH concentration on wetting time**

The percentage swelling of the formulations varied from 204.03 ± 5.50 to 303.31 ± 9.15 %. A very important relationship (p=0.0001), characterized by a positive correlation coefficient (R2=0.9881), was observed between the level of TPOH and percentage swelling, suggesting that higher concentrations of TPOH led to an increase in percentage swelling. The highest percentage of swelling was observed in the formulation with 15% of TPOH. Comparable outcomes were observed when the swelling study was conducted in 0.1 M HCl and phosphate buffer at pH 7.4. The impact of TPOH concentration on swelling (%).

1

10

100

1000

1

2

3

4

5

6

7

Concentration of TPOH (%)

Swelling (%)

**Figure: Effect of TPOH concentration on percentage swelling**

* **CONCLUSION**

The results indicate that both treated Plantago ovata husk (TPOH) and pregelatinized suji (Psuji) meet the criteria for disintegrants in fast dissolving tablets. Treated Plantago ovata husk and pregelatinized suji have demonstrated superior disintegrant properties compared to synthetic super disintegrants (like sodium starch glycolate) and those available on the market. Consequently, these formulations can be investigated further in clinical trials and later for commercialization, as they may serve as improved alternatives to current conventional products on the market.

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