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# FORMULATION AND EVALUATION OF METFORMIN ORODISPERSIBLE TABLETS

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***Abstract:***

*This study, the effect of using variable quantity of disintegrating agents like Crossceramilosesodium, Crospovi done, Sodium Starch Glycolate on the mouth dissolving property of Metformin tablets. Total five formul ations in triplicate having disintegrants at variable amount were prepared by direct compression method. The tablets, were assessed if suitable as oral disintegrating tablets by determination of a range of technological parameters. Tablets were prepared by direct compression method and evaluated for hardness, thickness, friability, disintegration time, and percentage of drug release. It was observed that the formulation containing SSG were have better disintegrating property compared to othe r. Hardness of the tablets was found to be in the range of 3.4-3.9 kg/cm$^2$ for all formulations. The wetting time d ecreased with the increase in concentration of disintegrants. The tablets showed 97.52 ±0.46 % to 100.56 ±0.3 2 % of the labeled amount of drug, indicating uniformity in drug content. The in vitro dissolution time of various formulations was between 26.6 ±1.22 secs to 45.6±2.57 secs.*

***Keywords:*** *Orodispersible tablets, Crospovidone, Sodium starch glycolate, Super disintegrants.*

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## INTRODUCTION

Most of the oral pharmaceutical dosage forms like conventional tablets and capsules are formulated to be swallowed or chewed. As a result children, bedridden patients and elderly patients have difficulty in swallowing these dosage forms. To overcome these drawback novel drug delivery systems like orally disintegrating tablets have been developed which disintegrate/dissolve/disperse in saliva within few seconds without water. United States of America Food and Drug Administration (USFDA) define ,ODT as A solid dosage form containing medicinal substances or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon a tongue [1].

The major advantage of the ODT formulation is that it combines the advantages of both liquid and conventional tablet formulations. It provides the convenience of a tablet formulation, and also allowing the ease of swallowing provided by the liquid formulation[1]. The various technologies used to prepare ODTs include direct compression, sublimation, tablet moulding, spray drying, freeze drying and mass extrusion [2,3,4].

Metformin Hcl is chemically (N,Ndimethylimidodic arbonimidic diamide hydrochloride) an orally administ ered hypoglycemic agent used in the treatment of no n-insulin-dependent diabetes8(Type 2). As the dose of the conventional tablet is high, it gives the problem of difficulty in swallowing. Other problems like hand tremors, dysphagia incase of geriatric patients and in ca se of non co-operative patients the problem of swallow ing is common phenomenon which leads to poor pati ent compliance. To overcome these drawbacks Mou th dissolving tablets or orally disintegrating tablets or Fast dissolving tablets has emerged as an alternative oral dosage form. On the basis of these considerations, in the present study it was proposed to formulate an oral delivery device, in the form of rapidly disintegrating tablets by using direct compression technology, with the aim of rapid disintegration and a complete drug release in a short period of time. The main effect and the interactions of disintegrants on dispersion time and drug release were studied.

## MATERIALS AND METHODS

Metformin was obtained as gift sample from Hetero Drugs

Pvt, Lactose, Crospovidone, Mannitol, Magnesium ste arate used were of Pharmacoepial grade. Croscarmellose, Crospovidone, Sodium Starch Glycolate (SSG), aspartame and flavour

where obtained from s.d fine chemicals. All chemicals used were of analytical grade.

**Preparation of Orally Disintegrating Tablets**

The orodispersible tablets were prepared by a direct compression method. The drug mixture was prepared by homogeneously mixing the Croscarmellose sodium, crospovidone, sodium starch glycolate, lactose, and mannitol. All the ingredients of the oro dispersible tablet of Metformin Hcl was weighed, sifted and mixed in mortar with the help of pastel, then in the last magnesium stearate and talc was added as lubricating agent. The mixture was then compressed using a 12.5 mm punch in a single stroke on single punch tablet machine. The final blend was mixed thoroughly for 2-3 minutes in the poly bag and tablets were compressed.

**PRE COMPRESSION PARAMETERS** [5, 6]

**Angle of Repose**

It is the maximum angle that can be obtained between the free standing surface of the granule heap and the horizontal plane. The angle of repose can be calculated by the following formula[6-8].

**Tanθ = h / r (or)**

**tan- = h/r**

Where **θ**, = Angle of repose, h = height of the pile, r = radius of plane surface occupy by the powder

**Bulk Density**

Granular powder weighing 10 g was placed in 100ml measuring cylinder. Volume occupied by the powder was noted without disturbing the cylinder and bulk density was calculated by the following equation.

Bulk density = weight of sample / Volume of packed

The experiment was repeated for three times.

**Tapped Density**

Granular powder weighing 10g was placed in 100ml measuring cylinder. The cylinder was then subjected for the fixed number of taps (100) until the powder bed has reached the minimum. The final volume was recorded and the tap density was calculated by the following equation.

True density = Mass of bulk sample / Volume of bulk drug on tapping

The experiment was repeated for three times.

**Carr's Index**

Carr's percent compressibility was calculated for granules prepared by using the equation

[d tap- d bul / d tap] x 100

Where, tap= Tapped density or True density, bul = Bulk density.

**Hausner ratio**

Tapped density and bulk density were determined and the Hausner ratio was calculated by the following formula,

Hausner ratio = d tap / d bul

Where, d tap= Tapped density or True density, d bul = Bulk density.

**Table1: Formulation Development of Metformin Hcl Oro Dispersible Tablets**

| Ingredients in mg | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| **Metformin Hcl** | 250 | 250 | 250 | 250 | 250 |
| **Lactose** | 70 | 70 | 70 | 70 | 70 |
| **Mannitol** | 90 | 90 | 90 | 90 | 90 |
| **Crospovidone XL** | 15(6%) | 12.5(5%) | 10(4%) | 7.5(3%) | 5(2%) |
| **Croscarmellose** | 12.5(5%) | 12.5(5%) | 12.5(5%) | 12.5(5%) | 12.5(5%) |
| **Sodium Starch Glycolate** | 5(2%) | 7.5(3%) | 10(4%) | 12.5(5%) | 15(6%) |
| **Aspartame** | 4.5 | 4.5 | 4.5 | 4.5 | 4.5 |
| **Mint flavour** | 1 | 1 | 1 | 1 | 1 |
| **Magnesium Stearate** | 2 | 2 | 2 | 2 | 2 |
| **Total weight (mg)** | **450** | **450** | **450** | **450** | **450** |

**EVALUATION OF TABLETS** [7-12]

**Thickness**

Thickness was determined for twenty pre-weighed tablets of each batch using a digital venire scale (Mitutoyo- Digi) and the average thickness was determined in mm**.** The tablet thickness should be controlled within a 5% variation of a standard.

**Hardness**

Hardness or crushing strength is the force required to break a tablet in diametric compression. Hardness of the tablets is determined by Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moving along the gauze in the barrel at which the tablet fractures indicates the hardness of the tablet. Six tablets from each batch were taken randomly and their hardness was determined.

**Friability**

This test is performed to evaluate the ability of a tablet to withstand abrasion in packing, handling and transporting purpose. Twenty sample tablets were rotated at 25rpm for 4 minutes by a USP-type Roche friabilator, then reweighed after removal of fines and the percentage weight loss was calculated according to the following formula. The tablets were found to pass the friability test, if the percentage weight loss was found to be less than 1%.

% Friability= $(W_0\text{-}W)/W_0$ x100

Where $W_0$=initial weight of twenty tablets

W= weight of 20 tablets after 100 revolutions

**Disintegrating Time**

The disintegration test is carried out in an apparatus (Electro lab, Mumbai) containing a basket rack assembly with six glass tubes of 7.75 cm in length and 2.15 mm in diameter, the bottom of which consists of a #10 mesh sieve. The basket is raised and lowered 28-32 times per minute in a medium of 900 ml which is maintained at 37 ± $2^0$C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh (#10) was considered as the disintegration time of the tablet. The disintegration time that patients can experience for oral disintegrating tablets ranges from 5 to 30 sec.

**Dissolution Study**

The release rate of Metformin hydrochloride Orodispersible tablets was determined using United States pharmacopeia (USP) Dissolution Testing Apparatus 2 (paddle method) .The dissolution test was performed using 900 ml of Phosphate buffer pH 6.8, at 37 ± 0.5C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus and the samples were replaced with fresh dissolution medium. The samples were filtered through filter paper. Absorbance of these solutions was measured at 233 nm using a UV/Visible Spectrophotometer. The drug release was plotted against time to determine the release profile.

**Stability Studies**

The optimized formulation was subjected for stability studies at accelerated conditions of a temperature $40^0$ C and a relative humidity of 75%

and at 0,10,20 and 30 days for their physical appearance, hardness, disintegration time, drug content, friability, thickness and %drug release.

## RESULTS AND DISCUSSION

Five formulations were designed; using higher and lower level of super disintegrants Crospovidone, croscarmellose sodium and sodium starch glycolate were used as super disintegrants. For each designed formulation, blend of drug and excipients were prepared and Oral disintegrating tablets of Metformin Hcl were prepared by direct compression method in different concentrations. Five formulations were prepared, the powder blend of five formulations F1 to F5 was evaluated for Angle of repose, Bulk density, Tapped density, Carr′s index and Hausner′s ratio, which showed the pre-compressed blend, has good flow property. The results are shown in Table 2.

The values of different physical tests are given in Table 3. The oro dispersible tablets obtained had drug contents in the range of 98 to 100%. This is within the acceptable limit. Hardness of tablet was found in the range of 3.10 to 3.45 kg/cm$^2$. Friability was found to be below 1% which indicates good mechanical strength of the tablets. All the formulations found to have much faster wetting time when compared to the control with significant increase in the water absorption capacity. The disintegration time (DT) for the formulation prepared with Sodium Starch glycolate, Croscarmellose and crospovidone was found to be in the range of 10-14 second. Among all the formulations, F4 was shown promising results as the DT was 10 second.

*In-vitro* drug release studies were performed with all formulations. The results are accordingly tabulated in Table 4 and Figure 1, 2. The percentage drug release for the formulation F4 was found 100% respectively at the end of 15 minutes. Formulation F4 prepared with sodium starch glycolate (5%), crospovidone (3%) and Croscarmellose (5%) was found to be the optimized formulation than other formulations.

The optimized formulation F4 were selected for accelerated stability studies and the tablets possessed the same parameters even after the stressed conditions, indicates good stability properties of formulation inTable 5.

**Table: 2 Evaluation of Directly Compressible Blend of Metformin Hcl**

| Formulation code | Bulk density(g/cc) | Tapped density(g/cc) | Car's Index | Hausner Ratio | Angle of repose |
|---|---|---|---|---|---|
| **F1** | 0.378 | 0.477 | 20-26 | 1.25 | 33.92º |
| **F2** | 0.407 | 0.528 | 16.91 | 1.31 | 31.25º |
| **F3** | 0.419 | 0.555 | 18.50 | 1.32 | 32.61º |
| **F4** | 0.461 | 0.596 | 17.97 | 1.26 | 30.61º |
| **F5** | 0.467 | 0.529 | 15.76 | 1.19 | 28.42º |

**Table: 3 Evaluations of Metformin Hcl Oro dispersible tablets**

| Formulation code | Average weight(mg) | Thickness(mm) | Hardness(Kp) | Percentage friability (%) | Disintegration time(sec) |
|---|---|---|---|---|---|
| **F1** | 203.0 | 3.21 | 1.09 | 1.56 | 13 |
| **F2** | 197.6 | 3.10 | 1.30 | 0.69 | 14 |
| **F3** | 200.0 | 3.41 | 2.86 | 0.16 | 12 |
| **F4** | 198.4 | 3.45 | 1.75 | 0.35 | 11 |
| **F5** | 198.0 | 3.37 | 2.21 | 0.17 | 13 |

**Table: 4 Cumulative Percentage Drug Release of Metformin Hcl**

| Time(Secs) | F 1 | F 2 | F 3 | F4 | F5 | Marketed product |
|---|---|---|---|---|---|---|
| **0** | 0 | 0 | 0 | 0 | 0 | 0 |
| **5** | 85.3 | 84.4 | 85.2 | 85.5 | 87.6 | 90.4 |
| **10** | 89.1 | 92.4 | 94.6 | 90.6 | 92.9 | 94.6 |
| **15** | 93.2 | 95.5 | 96.6 | 98.5 | 97.0 | 96.2 |

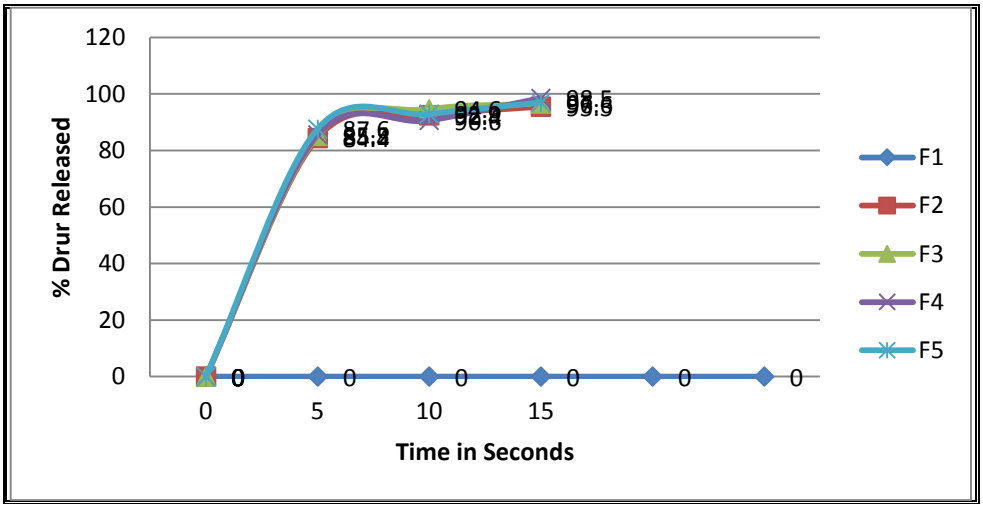


**Fig: 1 Dissolution Profile F1-F5**

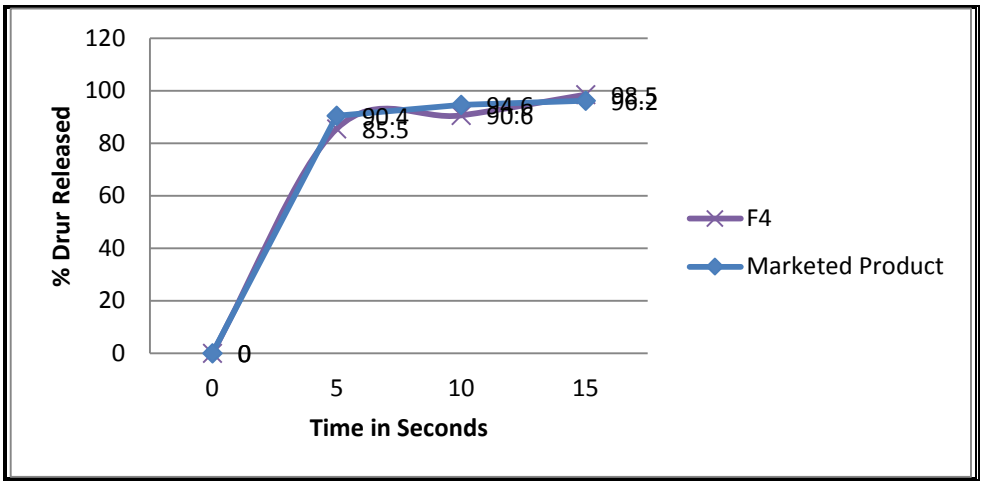


**Fig: 2 Dissolution profile of F4 and Marketed product (R)**

**Table 5: Accelerated Stability Studies of the Optimized Batch at 40oC/75%RH**

| S.No | Parameters | Initial | 15 days | 30 days |
|---|---|---|---|---|
| **1** | Average weight of Tablet (mg) | 430.2 | 430.3 | 430.3 |
| **2** | Thickness (mm) | 4.2 | 4.2 | 4.3 |
| **3** | Hardness (kp) | 3.2 | 3.3 | 3.3 |
| **4** | Friability (%) | 0.38 | 0.37 | 0.38 |
| **5** | Disintegration time in seconds | 9 | 9 | 10 |
| **6** | Drug content (%) | 101 | 102 | 101 |
| **7** | %Drug release(at 15 sec) | 99.3 | 100 | 100.2 |

## CONCLUSION

On the basis of evolutionary result of pre compression and post compression studies of all the formulation, we conclude that all the technological / evolutionary parameters of mouth dissolving tablet of Metformin Hcl with various super disintegrants. Among that the crospovidone is having the better disintegrating property.

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