Research Article

# Preparation and *In - Vitro* Evaluation of Glyburide Fast Dissolving Tablets by Using Solid Dispersion Technique

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**ABSTRACT**

Glyburide belongs to class II drugs, that is, characterized by low solubility and high permeability therefore, the enhancement of its solubility and dissolution profile is expected to significantly improve its bioavailability and reduce its side effects. The precompression blend of Glyburide soild dispersions were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio**.** The precompression blend of all the batches indicates well to fair flow ability and compressibility. Solid dispersions were prepared with various concentrations of carriers; the prepared solid dispersions were compressed into tablets. The formulated tablets were evaluated for various quality control parameters. The tablets were passed all the tests. Among all the formulations F2 formulation containing, Drug and β cyclodextrin in the ratio of 1:2 showed good result that is 97.06 % in 20 minutes. Hence from the dissolution data it was evident that F2 formulation is the better formulation. By conducting further studies like *Invivo* studies, preclinical and clinical studies we can commercialize the product.

**Keywords:** Glyburide, solid dispersions, β cyclodextrin.

## INTRODUCTION

The oral route of administration is considered as the most widely accepted route because of its convenience of self-administration, compactness and easy manufacturing.[1-2] But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patients incompliance particularly in case of pediatric and geriatric patients[1], but it also applies to people who are ill in bed and to those active working patients who are busy or travelling, especially those who have no access to water[2.] A Fast dissolving tablet (FDT) is a solid dosage form that contains medicinal substances and disintegrates rapidly (within seconds) without water when placed on the tongue. The drug is released, dissolved, or dispersed in the saliva, and then swallowed and absorbed across the GIT.[4] US FDA defined FDT tablets as "A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue". Recently European Pharmacopoeia used the term 'Fast dissolving tablet' as a tablet that is to be placed in the Fast where it disperses rapidly before swallowing. Fast dissolving tablets are also called as Fast -dissolving tablets, fast disintegrating tablets, fast dissolving tablets, fast dissolving tablets, rapimelts, porous tablets, quick dissolving tablet[5].An FDT may have varying degrees of pre gastric absorption of drugs and thus, the pharmacokinetic profiles of drugs will vary, therefore, the FDTs will not be bioequivalent to the conventional dosage forms. The ideal characteristics of a drug to develop as an FDT include:

No bitter taste, Small to moderate molecular weight, Good stability in water and saliva, Partially non-ionized at the oral cavities Ph, Ability to diffuse and partition into the epithelium of the upper GIT (log P > 1, or preferably > 2), Ability to permeate oral mucosal tissue, Dose should be low as possible.

### Unsuitable drug characteristic for FDTs:

Short half-life and frequent dosing, Very bitter or otherwise unacceptable taste because taste masking cannot be achieved, required controlled or sustained release.

## MATERIALS

Glyburide were purchased in SURA Labs, B-Cyclodextrin, SSG, CCS, CPV, and Microcrystalline Cellulose was purchased in Nihar traders' pvt Ltd, Sodium hydroxide, Magnesium stearate was purchased Himedia Laboratories, Potassium dihydrogen-ortho phosphate, and talc was purchased Finar chemicals Ltd.

## METHODOLOGY

### Preformulation Studies

Preformulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterized with the goal of designing optimum drug delivery system.

### Determination of absorption maxima

A spectrum of the working standards was obtained by scanning from 200-400nm against the reagent blank to fix absorption maxima. The λmaxwas found to be 255nm. Hence all further investigations were carried out at the same wavelength.

**Formulation Development**

Solid dispersions were prepared by solvent evaporation method. Methanol was used as solvent. Glyburide was taken as 50 mg. Water soluble polymers such as β cyclodextrin was selected as carriers. Drug and polymers were taken in different ratios stated in the formulation chart (Table). The prepared solid dispersions were passed through the sieve no #20 to get uniform sized particles. The solid dispersions were mixed with required quantities of diluent, lubricant and glidant. The blend was evaluated for precompression parameters.

| Ingredients (mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Drug equivalent to 10 MG | 20 SD1 | 30 SD1 | 40 SD1 | 20 SD2 | 30 SD2 | 40 SD2 | 20 SD3 | 30 SD3 | 40 SD3 |
| SSG | 30 | 30 | 30 | - | - | - | - | - | - |
| CCS | - | - | - | 30 | 30 | 30 | - | - | - |
| CP | - | - | - | - | - | - | 30 | 30 | 30 |
| Mg.Stearate | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| MCC | QS | QS | QS | QS | QS | QS | QS | QS | QS |

Total weight of tablets = 100 mg, the tablets were prepared by using 6 mm flat surfaced punch. The hardness of the tablets was maintained as 2 to 2.5 kg/cm$^2$.

## RESULTS AND DISCUSSION

**Determination of λ max**

The prepared stock solution was scanned between 200-400 nm to determine the absorption maxima. It was found to be 255 nm.

**Calibration curve of Glyburide**

The standard curve of Glyburide was obtained and good correlation was obtained with $R^2$ value 0f 0.999.the medium selected was pH 6.8 phosphate buffers. The standard graph values of Glyburide are tabulated as below-

**Standard Graph values of Glyburide at 255 nm in pH 6.8 phosphate buffer**

**Table : 2** standard graph values

| Concentration (µg/ml) | Absorbance |
|---|---|
| 0 | 0 |
| 2 | 0.198 |
| 4 | 0.396 |
| 6 | 0.601 |
| 8 | 0.804 |
| 10 | 0.998 |

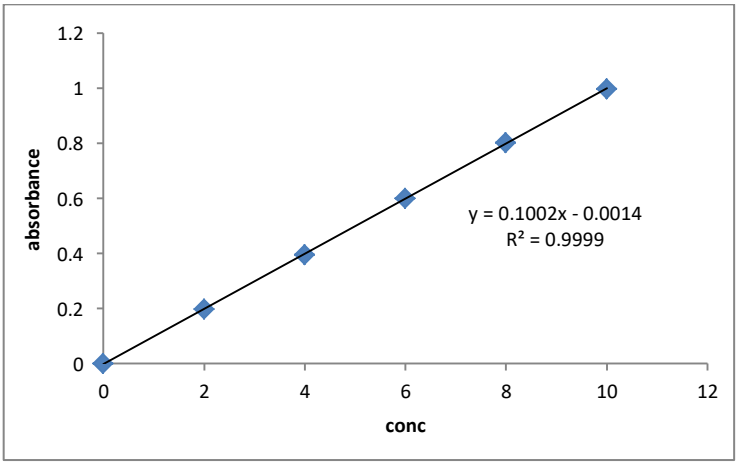


**Fig no 1:** Standard Curve f Glyburide

**Table 3:** Physical properties of precompression blend:

| Formulation Code | Angle of repose (Θ) | Bulk density (gm/cm$^3$) | Tapped density (gm/cm$^3$) | Carr's Index (%) | Hausner's ratio |
|---|---|---|---|---|---|
| F1 | 25.10° | 0.53 | 0.59 | 9.43 | 1.11 |
| F2 | 25.43° | 0.54 | 0.60 | 9.40 | 1.10 |
| F3 | 25.41° | 0.54 | 0.58 | 10.01 | 1.07 |
| F4 | 26.40° | 0.51 | 0.61 | 10.11 | 1.19 |
| F5 | 27.12° | 0.58 | 0.63 | 10.34 | 1.08 |
| F6 | 25.31° | 0.59 | 0.64 | 10.12 | 1.08 |
| F7 | 26.11° | 0.56 | 0.63 | 9.93 | 1.12 |
| F8 | 26.15° | 0.53 | 0.58 | 10.13 | 1.09 |
| F9 | 26.10° | 0.54 | 0.61 | 10.2 | 1.12 |

**Table 4:** Physical Evaluation of Glyburide tablets:

| Formulation code | Weight variation (mg) | Thickness (cm) | Hardness (Kg/cm$^2$) | Friability (%) | Content uniformity (%) |
|---|---|---|---|---|---|
| F1 | 103.12 | 4.76 | 2.5 | 0.420 | 99.12 |
| F2 | 98.56 | 4.74 | 2.2 | 0.341 | 99.03 |
| F3 | 99.67 | 4.71 | 2.1 | 0.363 | 100.01 |
| F4 | 97.23 | 4.80 | 2.1 | 0.561 | 100.31 |
| F5 | 109.09 | 4.81 | 2.0 | 0.482 | 99.63 |
| F6 | 105.24 | 4.74 | 2.2 | 0.513 | 99.41 |
| F7 | 100.23 | 4.76 | 2.2 | 0.412 | 97.94 |
| F8 | 99.73 | 4.71 | 2.3 | 0.432 | 96.16 |
| F9 | 98.34 | 4.73 | 2.5 | 0.512 | 100.15 |

***In-vitro* release studies:** The drug release rate from tablets was studied using the USP type II dissolution test apparatus. The dissolution medium was 500 ml of pH 6.8 phosphate buffer at 50 rpm at a temperature of 37 ± 0.5 °C. Samples of 5 ml were collected at different time intervals up to 1 hrs and analysed after appropriate dilution by using UV Spectrophotometer at 254nm.

**Table No 5:** In-vitro dissolution data for formulations F1 – F9.

| Time(MIN) | % Drug release | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 5 | 16.73 | 26.73 | 22.56 | 28.86 | 23.18 | 19.21 | 20.86 | 26.18 | 19.21 |
| 10 | 20.4 | 41.06 | 46.57 | 39.01 | 41.86 | 32.60 | 36.01 | 45.86 | 22.60 |
| 15 | 45.9 | 74.9 | 68.9 | 48.16 | 66.06 | 56.43 | 41.16 | 55.06 | 46.43 |
| 20 | 65.56 | 97.06 | 87.73 | 60.22 | 81.44 | 64.83 | 50.22 | 76.44 | 54.83 |
| 25 | 74.9 | | 92.4 | 76.99 | 99.62 | 71.32 | 66.99 | 80.62 | 61.32 |
| 30 | 84.4 | | | 88.81 | | 87.95 | 78.81 | 88.45 | 80.95 |

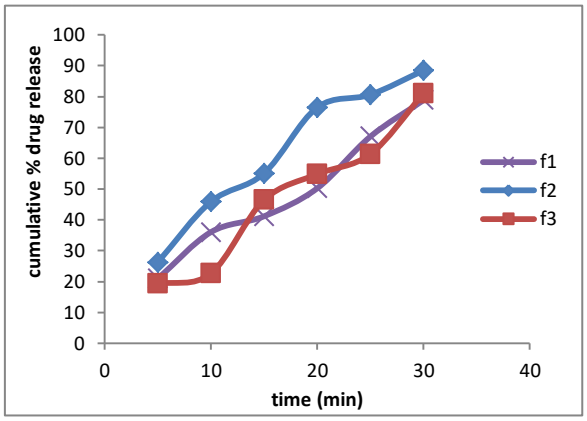


**Figure: 2** *In-vitro* dissolution data for formulations F1 – F3

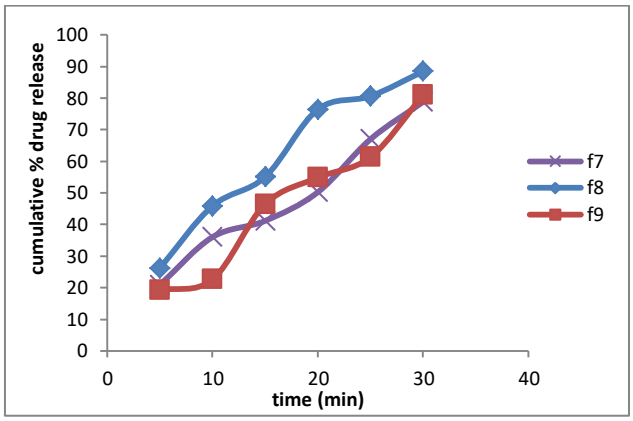


**Figure 3:** *In-vitro* dissolution data for formulations F7– F9.

Among all the formulations F2 formulation containing, Drug and β cyclodextrin in the ratio of 1:2 showed good result that is 97.06 % in 20 minutes, the concentration of super disintegrants is 30 mg. As the concentration of polymer increases the drug release was decreased. Hence from the dissolution data it was evident that F2 formulation is the better formulation. The formulation is following zero order release kinetics.

## SUMMARY AND CONCLUSION

Glyburide belongs to class II drugs, that is, characterized by low solubility and high permeability therefore, the enhancement of its solubility and dissolution profile is expected to significantly improve its bioavailability and reduce its side effects. The standard curve of Glyburide was obtained and good correlation was obtained with $R^2$ value 0f 0.999.the medium selected was pH 6.8 phosphate buffers, The precompression blend of Glyburide solid-dispersions Immediate release tablets by using super disintegrants were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio**.** The precompression blend of all the batches indicating good to fair flow ability and compressibility. Among all the formulations F2 formulation containing, Drug and β cyclodextrin in the ratio of 1:2 showed good result that is 97.06 % in 20 minutes. Hence from the dissolution data it was evident that F2 formulation is the better formulation.

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