# FOMULATION AND EVALUATION OF GASTRORETENTIVE MUCOADHESIVE SUSTAINED RELEASE OF GLIPIZIDE TABLETS

S SHOBHA RANI*, KAMSANI SRAVANI
Centre for pharmaceutical sciences,
institute of science and technology,jawaharlalnehru technological university kukutpally,
telangana, 500085,india.

**Abstract**

**Glipizide is An oral hypoglycemic agent which is rapidly absorbed and completely metabolized.Glipizide is a anti-diabetic medicine which is used to type 2 diabetics.The effectiveness of Glipizide extended-release tablets in type 2 diabetes at doses from 5– 60 mg once daily has been evaluated in 4 therapeutic clinical trials each with long-term open extensions involving a total of 598 patients. Once daily administration of 5, 10 and 20 mg produced statistically significant reductions from placebo in hemoglobin A1C, fasting plasma glucose and postprandial glucose in patients with mild to severe type 2 diabetes.**

**Keywords; Gastroretensive. Glipizide ,Optimized , polymers .**

**INTRODUCTIONS ;**

**Oral route of administration is the most important and convient route for drug delivery. This is mainly due to the fact that the extent of drug absorption from GIT is determined by GI Physiology ,irrespective of the control release properities of the device prolonged gastric retention improves bioavailability.**

**Sustain release dosage form are the formulation which release the therapeutically active agents for longer period of time at expected rate after its single dose administration.when hightly water soluble drugs are prepared as oral sustained release dosage form form cause problems like they may be releaseed more rapidly and results in toxicity if not prepared in appropriate fashion.**

**Glipizide appears to lower blood glucose acutely by stimulating the release of insulin from the pancreas, an effect dependent upon functioning beta cells in the pancreatic islets. Extrapancreatic effects also may play a part in the mechanism of action of oral sulfonylurea hypoglycemic drugs. Two extrapancreatic effects shown to be important in the action of Glipizide are an increase in insulin sensitivity and a decrease in hepatic glucose production. However, the mechanism by which Glipizide lowers blood glucose during long-term administration has not been clearly established. Stimulation of insulin secretion by Glipizide in response to a meal is of major importance. The insulin tropic response to a meal is enhanced with Glipizide administration in diabetic patients.**

**MATERIALS AND METHODS**

| Sr.No. | *Material* | Grade | Supplier |
|---|---|---|---|
| 1. | Glipizide | Pharma | Free sample |

| | | | |
|---|---|---|---|
| 2. | HPMCK4M | Pharma | Alkem pharmaceutical, Mumbai |
| 3. | Carbopol934 | Pharma | Alkem pharmaceutical, Mumbai |
| 4. | Sodium CarboxyMethyl Cellulose | Pharma | S.D.FineChem.Ltd |
| 5. | $NaHCO_3$ | A.R | S.D.FineChem.Ltd |
| 6. | Talc | AR | S.D.FineChem.Ltd |
| 7. | Magnesium stearate | AR | S.D.FineChem.Ltd |

**Details of Equipments Used**

| **Sr.No.** | Instrument | **Manufacturer** |
|---|---|---|
| 1. | Electronic Balance | Sartorius, Germany. |
| 2. | Tablet Compression Machine | Lab Press |
| 3. | Pfizer Hardness Tester | Pfizer |
| 4. | Friability Test Apparatus | Roche Friabilator. |
| 5. | Screw gauge micrometer | Elves |
| 6. | Tablet Dissolution Tester | Electro Lab.(USPXXIII) (DTD– 06P) |
| 7 | UV Spectrophotometer | Systolic |
| 8 | FTIR Spectrophotometer | perkinElmer |
| 9 | Scanning Electron Microscope | - |

| | | |
|---|---|---|
| 10 | Digital pH meter | Hemma |
| 11 | Hot Air Oven | Lawrence & Mayo. |
| 12 | Mucoadhesion Testing Assembly | Locally Modified |
| 13 | Vernier califer scale | - |

**OBJECTIVE OF WORK**

Preparation of standard curve of GLIPIZIDE

- Drug-Excipients compatibility study by FTIR spectrophotometer.
- Development of Gastro-retentive mucoadhesive tablets using Carbopol 934P, HPMCK4M,&sodiumCMC in different concentrations by direct compression method.
- To determinate the %drug release studies by diffusion
- To determinate the swelling index
- To perform the stability study

**Preparation of standard curve of Glipizide (in 0.1NHCL).**

**Procedure:**

***Preparation of standard solution:***

100mg of Glipizide was accurately weighed in to 100ml volumetric flask. The volume was made up with the0.1NHCL(pH 1.2)to get a concentration of 1000µg/ml (stock- I).From is10ml was with drawn and diluted to100ml to get a concentration of 100µg/ml(Stock-II)

***Preparation of working standard solutions***:

From (Stock-II) aliquots of 1ml, 2ml, 3ml,……..10 ml were pipette into 100ml volumetric sflasks. The volume was made up with distilled water to get the final concentration of 1, 2, 3.,,,,,12 µg/ml respectively. The absorbance of each concentration was measured at 267nm.

The data are compiled in Table and figure 1.

## COMPATABILITY STUDIES

### IR spectrum

Bruker FTIR Spectrometer is used to scan and characterize the IR spectra of various combinations of drug, excipients and optimized formulations in the present study and check the compatibility between drug (Glipizide) and various excipients. KBr pellet strategy is utilized for making pellets with help of weight of 8 to 10 tons in a KBr press and later scanning the pellets in instrument with help of OPUS programming the works in a state of harmony with the instrument. Range was checked shape 4000 to 400cm-1.(FIGURE NO 2-7)

## FORMULATION DESIGN

### Preparation of mucoadhesive tablets:

Mucoadhesive tablets were fabricated by wet direct compression method using formula show in Table**.** The drug and polymers were separately passed through sieve no. 40 and 60, respectively and mixed for 5 min in mortar with pestle. Lubricated with magnesium stearate by mixing at a slow speed for 5 min and compressed using 12.5mm flat punches in lab pess tablet compression machine to get tablets of 215 mg weight. The resulting mucoadhesive tablets were subjected to various evaluation parameters.

| DRUG | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Glipizide | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| HPMC K4M | 150 | - | - | 150 | - | | 75 | 75 | |
| SODIUM CMC | - | 150 | | | 150 | | 75 | | 75 |
| CARBOPOL937 | | | 150 | | | 150 | | 75 | 75 |
| ETHYl CELLULOSE | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| Mg sterate | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| talc | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Total** | **215** | **215** | **215** | **215** | **215** | **215** | **215** | **215** | **215** |

**VALAUTION OF PRE COMPRESSION PARAMETER;**

All the prepared mucoadhesive tablets were evaluated for following parameters.

- Angle of repose
- Bulk density
- Tapped density
- Compressibility index
- Hausner ' s ration

**Angle of repose ;**

Angle of repose was determined by using funnel method. The weighted powder was taken in a funnel. The height of the funnel was adjusted in such a way that the trip of the funnel just touches the apex of the heap of powder. The drug-excipient powder was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation and the results were given.

$$\tan \Theta = h / r$$

Where ;

h = height r = radius of the powder cone.

The results are presented in Table: 2

**LIMITS**

| **Angle of repose** | **Type of flow** |
|---|---|
| <25 | Excellent |
| 25 -30 | Good |
| 30-40 | Passable |

| | |
|---|---|
| >40 | Very poor |

**Bulk Density:**

It refers to a measurement to describe packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in mg/ml.

Procedure:

Weighed quantity of API was transferred into 100 ml measuring cylinder without tapping during transfer. The volume occupied by DRUG was measured. Bulk density was measured by using formula.

Bulk density =weight of the powder /initial volume

The results are presented in Table: 2

**Tapped Density:**

Procedure:

Weighed quantity of API was taken into a graduated cylinder. Volume occupied by DRUG was noted down. Then the cylinder was subjected to 500, 750 & 1250 taps in tap density tester (Electro Lab USP II). According to USP, the blend was subjected for 500 taps. % Volume variation was calculated and subjected for additional 750 taps. % Variation is calculated.

Tapped density = weight of the powder / final volume

The results are presented in Table: 2

**Compressibility Index:**

Weighed API was transferred to 100ml-graduated cylinder and subjected to 500,750&1250 taps in tap density tester (Electro lab). The difference between two taps should be less than 2%. The %of compressibility index calculated using formula.

CI = (initial volume – final volume ) / initial volume x 100

The results are presented in Table: 2

**Limits :**

| S.No | Compressibility index | Type of flow |
|---|---|---|
| 1 | 5-12 | Free flow |
| 2 | 12-16 | Good flow |
| 3 | 18-21 | Fair |

| | | |
|---|---|---|
| 4 | 23-25 | Poor |
| 5 | 33-38 | Very poor |
| 6 | >40 | Extremely poor |

**Hausner' s Ratio:**

It is measurement of frictional resistance of the drug. The ideal range should be 1.2 – 1.5.it is the determined by the ratio of tapped density and bulk density.

Hausner ' s ration = Tapped density / bulk density

**Limits ;**

**< 1.25 – good flow**

**> 1.25 - foor flow**

The results are presented in Table: 4

**EVALUATION OF POST COMPRESSION PARAMETERS**

- **Thinkness**
- **Hardness**
- **Weight variation**
- **Drug content uniformity**
- **Dissolution time**
- **Swelling index**
- **Stability studies**

**Thickness:**

Thickness was measured using a micrometer screw guage formulation were picked randomly and thickness was measured individually.

The results are given in Table: 3

**Hardness:**

Hardness was measured using Pfizer hardness tester. For each batch five tablets were tested.

The results are presented in Table: 3

**Friability:**

10tablets were weighed and placed in the Roche friabilator and apparatus was rotated at 25rpm for 4minutes. After revolutions, the tablets were dedusted and weighed again.The percentage friability was

measure dusing formula,

$$\%F=\{1-(Wt/W)\}\times 100$$

Where, %F= Friability in percentage

W = Initial weight of tablet
Wt= Weight of tablets after revolution

The results are given in Table: 3.

**Weight variation**:

Ten tablets were randomly selected from each batch and . The average weight and standard deviation of 20tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviate from the average weight by more than the percentage shown in and none deviate by more than twice the percentage shown.

The results are presented in Table: 3

**Drug content uniformity:**

Weigh and powder 10 tablets. Weigh accurately a quantity of powder containing about 10g of Glipizide transfer to 100ml volumetric flask. Add about 75ml of ethanol (95%) and shake for15min.dilute the volume with ethanol (95%) mix and filter. dilute 5ml of filtrate to 50ml with ethanol (95%) measure the absorbance of resulting solution at maximum 267nm.

The results are given in Table: 3

**INVITRO DISSOLUTION STUDIES OF TABLETS:**

Dissolution studies were carried out for all the formulations combinations in triplicate, employing USP XXVII paddle method and 900 ml of pH 6.8 phosphate buffers as the dissolution medium. The medium was allowed to equilibrate to temp of 37°c $\pm$ 0.5°c. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hrs in pH 6.8 phosphate buffer at 50 rpm. At definite time intervals of 5 ml of the aliquot of sample was withdrawn periodically and the volume replaced with equivalent amount of the fresh dissolution medium. The samples were analyzed spectrophotometrically at 235 nm using uv-spectrophotometer.

**Dissolution parameters:**

| | | |
|---|---|---|
| Apparatus | -- | USP-II, |
| Dissolution Medium | -- | pH 6.8 phosphate buffer |

| | | |
|---|---|---|
| RPM | -- | 50 |
| Sampling intervals | -- | 0.5,1,2,3,4,5,6,7,8,10,11,12. |
| Temperature | -- | 37°c ± 0.5°c |

The results are given in table; 4 and figure no ; 8

**Release Kinetics :**

The analysis of drug release mechanism from a pharmaceutical dosage from is an important but complicated process and is practically evident in the case of matrix systems. As a model-dependent approach, the diolution data was fitted to five popular release models such as zero-order, first-order, diffusion and exponential equations, which have been described in the literature. The order of drug release from matrix systems was described by using zero order kinetics or first orders kinetics. The mechanism of drug release from matrix systems was studied by using Higuchi equation, erosion equation and Peppas-Korsemeyer equation.

The results are given in Table; 5

**Zero Order Release Kinetics:** It defines a linear relationship between the fraction of drug released versus time.

$$Q = k_o t$$

Where, Q is the fraction of drug released at time t and $k_o$ is the zero order release rate constant.

A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

**First Order Release Kinetics:** Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that drug release from most of the slow release tablets could be described adequately by apparent first-order kinetics. The equation that describes first order kinetics is

$$\text{In } (1-Q) = - K_1 t$$

Where, Q is the fraction of drug released at time t and $k_1$ is the first order release rate constant.

Thus, a plot of the logarithm of the fraction of drug remained against time will be linear if the release obeys first order release kinetics.

**Higuchi' s equation:**

It defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time.

$$Q=K_2 t^{½}$$

Where, K2 is the release rate constant.

A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick' s law, square root time dependant.

**Power Law:**

In order to define a model, which would represent a better fit for the formulation, dissolution data was further analyzed by Peppas and Korsemeyer equation (Power Law).

$M_t/M_\alpha = K.t^n$

Where, $M_t$ is the amount of drug released at time t and $M_\alpha$ is the amount released at time $\alpha$, thus the $M_t/M_\alpha$is the fraction of drug released at time t,k is the kinetic constant and n is the diffusional exponent. To characterize the mechanism for both solvent penetration and drug release n can be used as abstracted in Table-6. A plot between log of $M_t/M_\alpha$ against log of time will be linear if the release obeys Peppas and Korsemeyer equation and the slope of this plot represents "n" value.

***SWELLING INDX·***

tablets were weighed individually (W1) and placed separately in 2% agar gel plates with the core facing the gel surface and incubated at 37°C ±1°C. At regular 1-hour time intervals until 10 hours, the tablet was removed from the Petri dish, and excess surface water was removed carefully with filter paper. The swollen tablet was then reweighed (W2) and the swelling index (SI) was calculated using the formula.

**% Swelling index = $[(W_2 - W_1)/W_1]\times 100$**

The results are given tablet ;7

**STABILITY STUDIES ;**

The accelerated stability study was performed on the selected formulas ( F1 T0 F9 ) which gave all most optimum results in all previous tests the test was carried out by placing the tablets of each selected formula in sealed punches and stored in thermostatically controlled ovens adjusted at different temperature ,namely ,40,50,60 ± 0.5 with relative humidity 75 % for 12 hr.Three tablets are selected each formula were taken from the ovens after 1,2,3,4,,,,,,,,,12 weeks.The stored tablets were examined visually for any change in colour appearance and analysed for determination of amount of drug remaining in each formula using HPLC stability – indicating method as previously mentioned.

The results listed in table ;8

**RESULTS AND CONCLUSION**

**PROPERITES**

| DISCRIPTION | GLIPIZIDE |
|---|---|
| Colour | White |
| Odour | Odourless |

| | |
|---|---|
| Test | Amorphous |

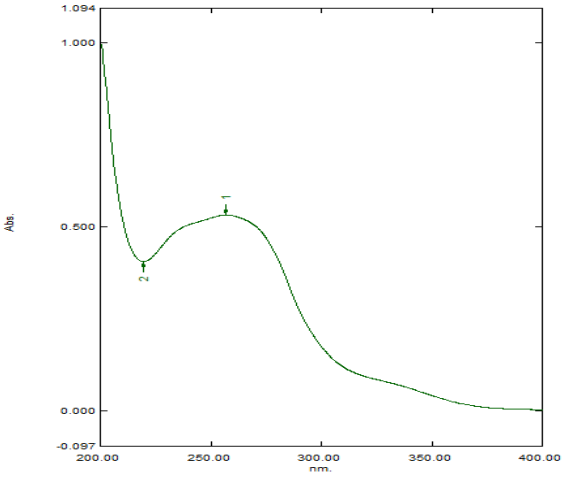
**SOLUBILITY PROFILE**

| SOLVENTS | GLIPIZIDE |
|---|---|
| Water | In soluble |
| Alcohol | In soluble |
| 0.1 NAOH | Soluble |
| 0.1N HCL | Soluble |
| Dimethyl formamide | Free soluble |

**STANDARD GRAPH OF GLIPIZIDE ( table no - 1)**

**ʎ Max was found to be 267 nm**

| Concentration | Absorbance |
|---|---|
| **0** | **0** |
| **2** | **0.078** |
| **4** | **0.217** |
| **6** | **0.279** |
| **8** | **0.372** |
| **10** | **0.458** |



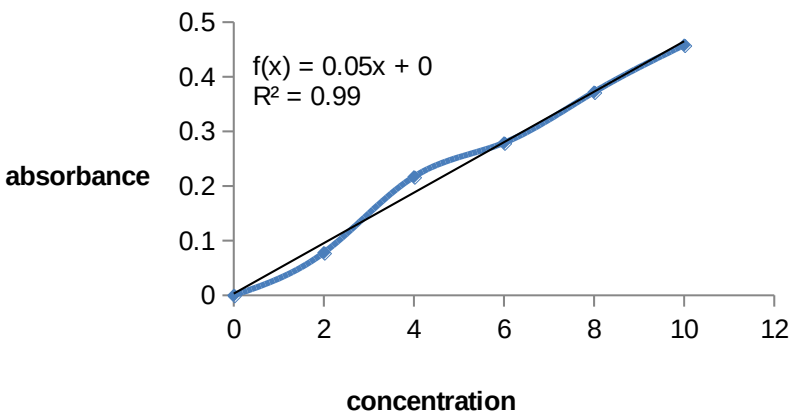
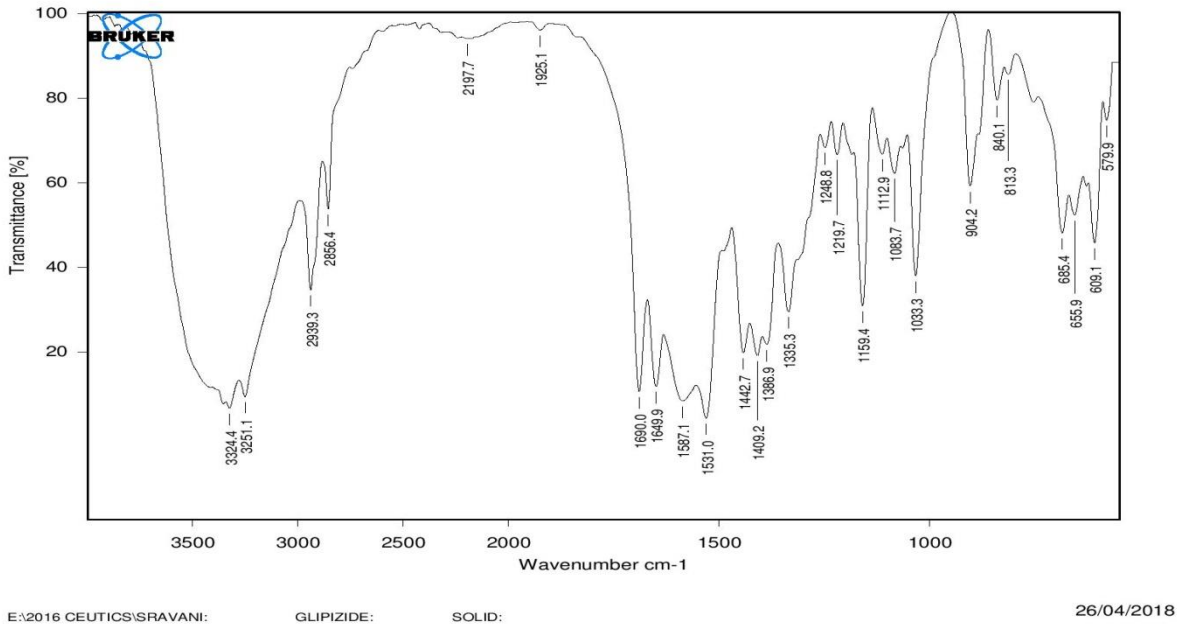




**Figure no-1**

**IR COMPATABILITY STUDY**

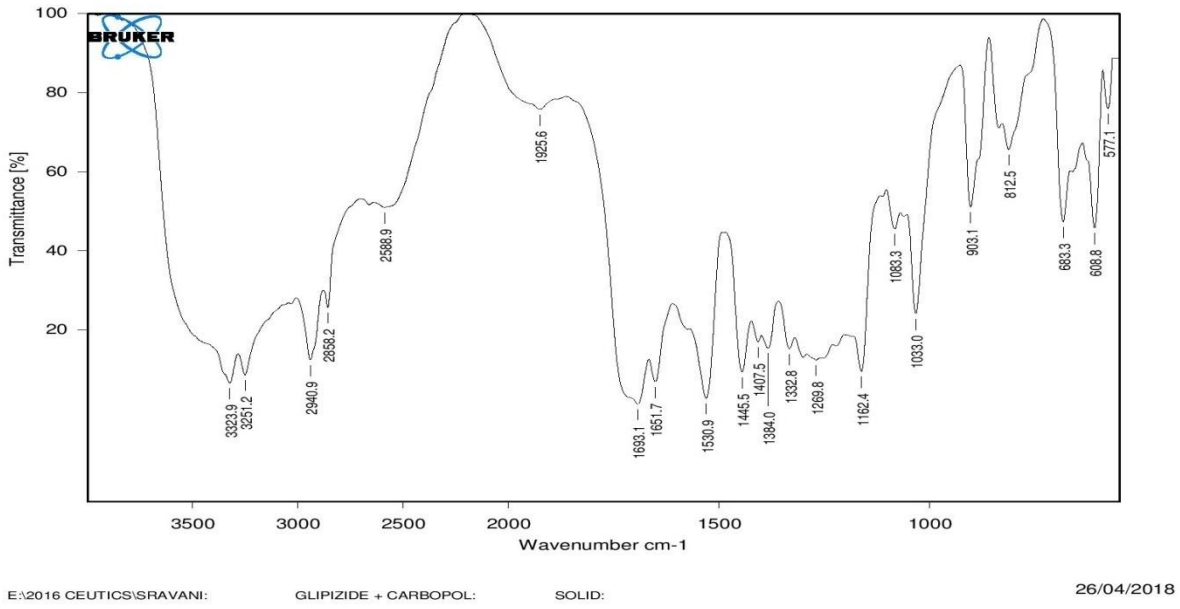
**IR SPETRUM OF GLIPIZIDE**

**figure no - 2**

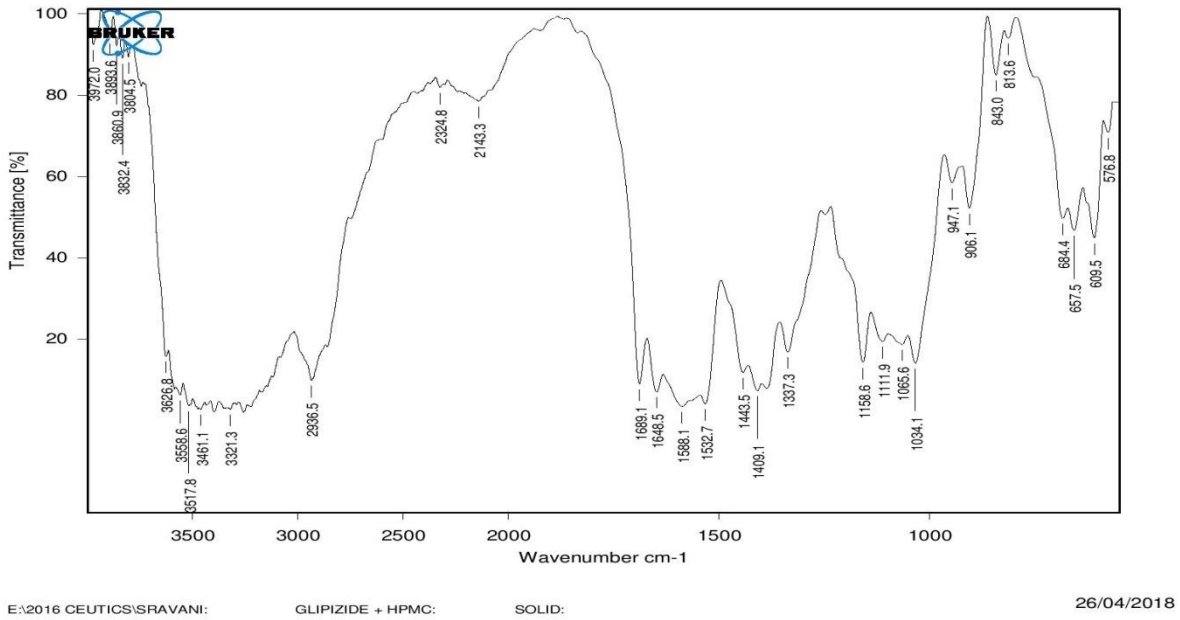



**IR SPECTRUM OF GLIPIZIDE +CARBOPOL 934**

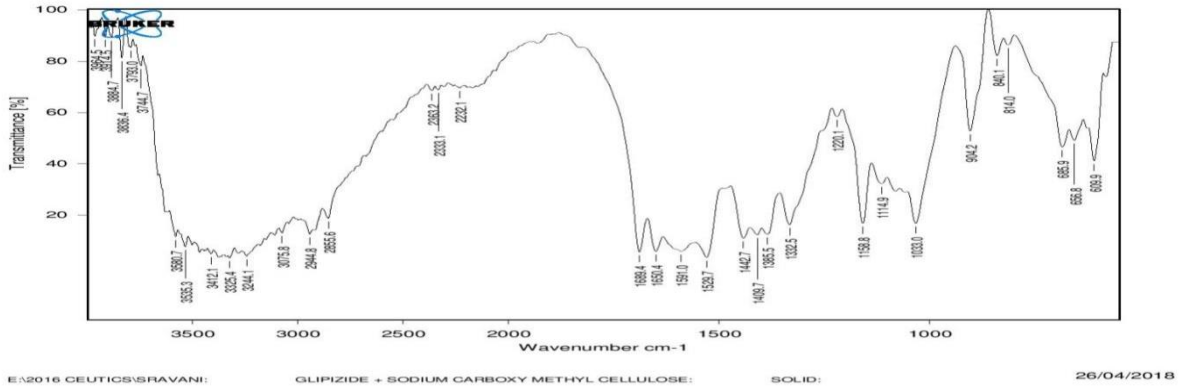
**figure no - 3**



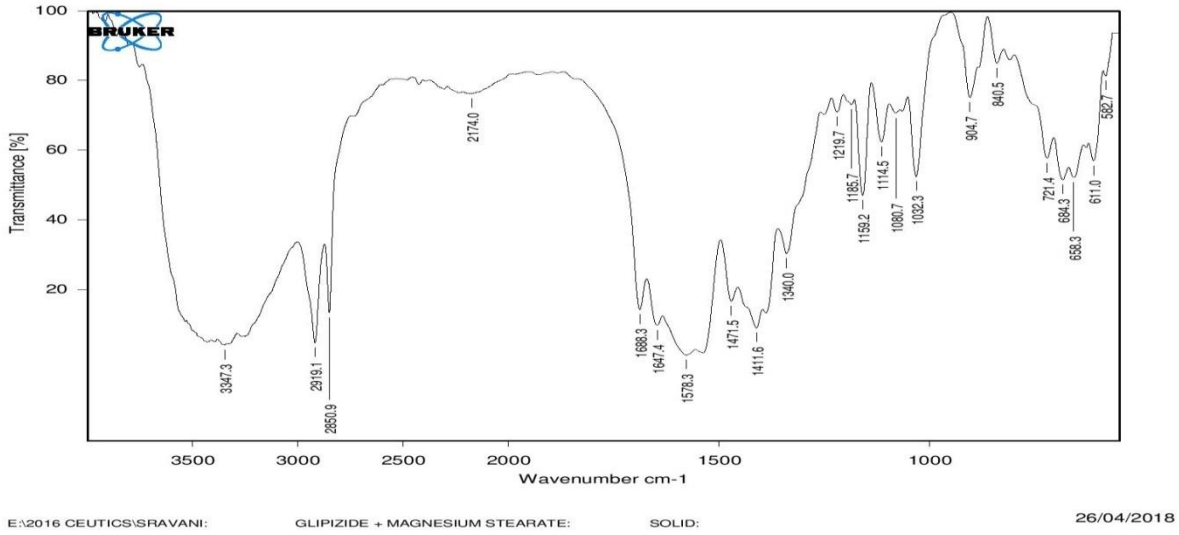

**IR SPECTRUM OF GLIPIZIDE +HPMC K4M (figure no - 4 )**



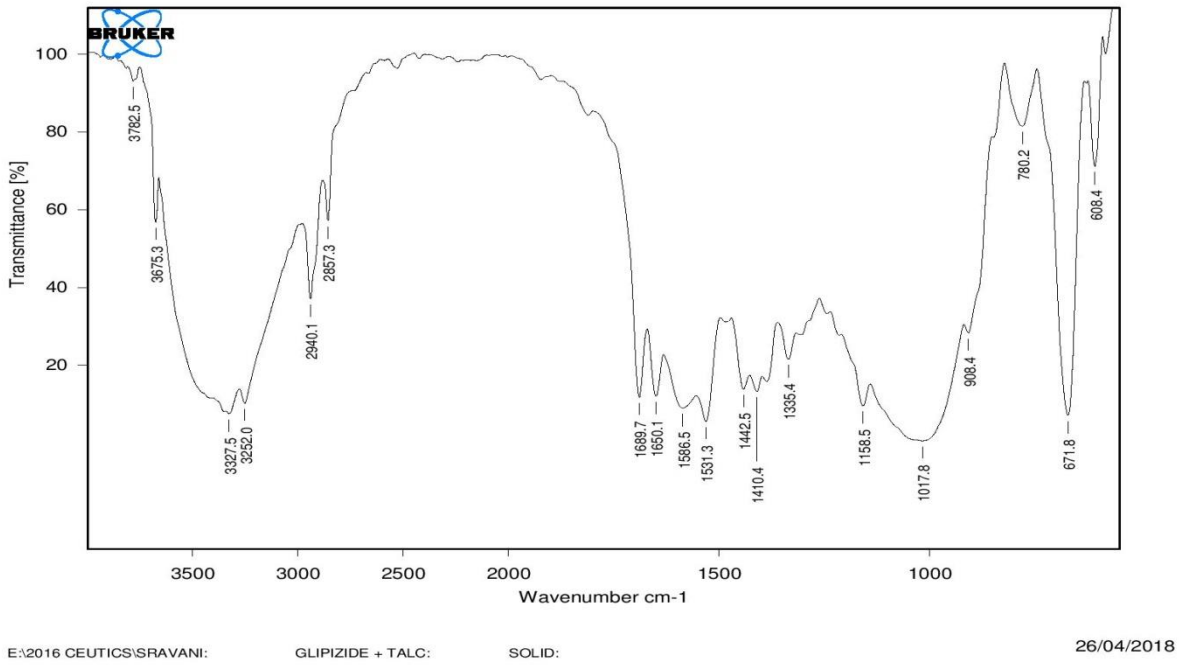

**IR SPECTRUM OF GLIPIZIDE + SODIUM CARBOXY METHYL CELLULOSE (figure no – 5)**




**IR SPECTRUM OF GLIPIZIDE + MAGNESIUM STEARATE ( figure no – 6)**




**IR SPECTRUM OF GLIPIZIDE + TALC (figure no – 7)**



**EVALUATION OF PRE COMPRESSIONAL PARAMETERS (Table no -2)**

| OPERITIES | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| ULK sity(gm/ml) | 0.56 ±0.01 | 0.58 ±0.01 | 0.56 ±0.04 | 0.55 ± 0.02 | 0.56 ± 0.01 | 0.57 ± 0.05 | 0.58 ± 0.04 | 0.57±0.06 | 0.59±0.01 |
| pped density n/ml) | 0.66±0.02 | 0.68± 0.04 | 0.65 ±0.03 | 0.64± 0.02 | 0.65 ± 0.02 | 0.66± 0.01 | 0.69± 0.01 | 0.67 ±0.02 | 0.69±0.05 |
| rr' s mpressibility ex (%) | 15.15±0.02 | 14.7 ±1.03 | 13.9 ±1.04 | 14.5 ± 1.02 | 13.8 ± 1.05 | 13.63 ± 1.15 | 14.7 ± 1.02 | 14.9 ±1.22 | 15.94 ± 0.83 |
| usner " s io | 1.16±0.03 | 1.15 ± 0.04 | 1.19 ± 0.05 | 1.16 ± 0.04 | 1.16 ± 0.04 | 1.15 ± 0.06 | 1.18 ± 0.02 | 1.17 ± 0.03 | 1.16 ±0.05 |
| gle of repose | 28.3±1.27 | 29.2 ± 1.04 | 25.8 ± 2.34 | 27.4 ± 1.95 | 27 ± 0.07 | 25.8 ± 0.03 | 26 ± 0.02 | 27.3 ± 0.04 | 26.5 ± 0.03 |

**Mean ± SD, n = 3**

**EVALUATION OF POST COMPRESSIONAL PARAMETERS (Table no -3**

| perity | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| rdness /cm²) | 5.1 ±0.57 | 5.2 ± 0.62 | 5.3 ±0.47 | 5.7 ± 0.72 | 5.5 ±0.46 | 5.6 ± 0.21 | 5.4±0.34 | 5.2 ±0.26 | 5.6 ±0.45 |
| ickness m) | 4.3 ±0.05 | 4.5 ± 0.07 | 3.6 ±0.62 | 4.7 ± 0.09 | 4.1 ±0.02 | 3.9 ±0.03 | 4.3±0.02 | 4.4 ± 0.09 | 4.2 ± 0.18 |
| ability ) | .31±0.03 | 0.36 ±0.05 | 0.39±0.1 | 0.42 ±0.09 | 0.37±0.15 | 0.38±0.14 | 0.41±0.24 | 0.40±0.34 | 0.35±0.56 |
| ight riation | 212.9±2.03 | 213.9± 3.06 | 214 ± 0.05 | 212.2 ±0.14 | 213.5 ±0.15 | 211.9 ± 0.16 | 214.3 ± 0.04 | 212.6 ± 0.05 | 213.3 ± 0.023 |
| ug ntent formity | 95.9 ± 1.36 | 97.4 ± 0.22 | 98.8 ±0.15 | 94.99 ±0.25 | 99.2 ± 0.13 | 100.1 ± 0.09 | 96.8 ± 0.56 | 99.8 ± 0.14 | 103.5 ± S0.04 |

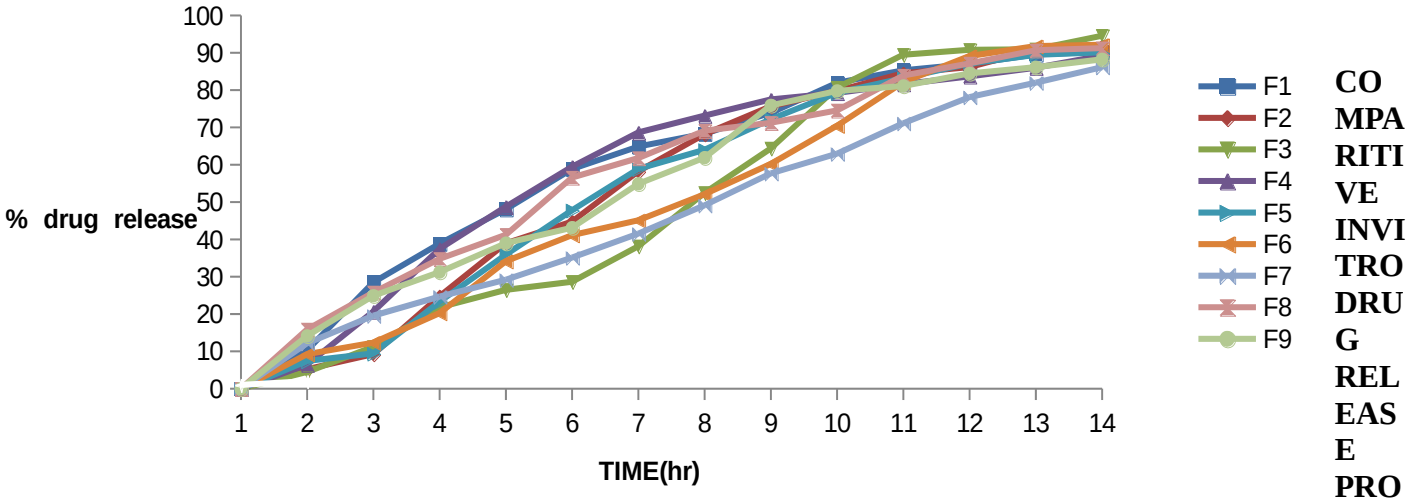
**Mean ± SD, n = 3**

**PERCENTAGE RELEASE FROM DIFFERENT FORMULATIONS(F1-F9S (TABLE NO – 4)**

| F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|
| 10.29±0.46 | 5.23±0.34 | 4.49±0.52 | 6.46±0.74 | 7.41± 0.56 | 9.23±0.67 | 12.15±0.56 | 15.88±0.12 | 14.13±0.23 |
| 28.48±0.78 | 9.23±0.68 | 11.19±0.47 | 20.67±0.68 | 9.43±0.23 | 12.34±0.65 | 19.560.34 | 25.78±0.34 | 24.89±0.13 |
| 38..87±0.24 | 24.75±0.47 | 21.79±0.64 | 37.46±0.48 | 23.3±0.67 | 20.24±0.65 | 24.67±0.45 | 34.78±0.43 | 31.23±0.23 |
| 48.09±0.22 | 38.96±0.84 | 26.48±0.74 | 48.76±0.64 | 35.9±0.34 | 34.14±0.23 | 29.19±0.34 | 41.23±0.68 | 38.99±0.78 |
| 58.86±0.09 | 44.76±0.48 | 28.64±1.06 | 59.49±0.84 | 47.8±0.78 | 41.12±0.11 | 35.12±0.34 | 56.56±0.34 | 43.14±0.68 |
| 64.86±0.75 | 58.23±0.57 | 38.16±1.04 | 68.64±0.98 | 58.9±0.45 | 45.12±0.22 | 41.53±0.34 | 61.78±0.22 | 54.88±0.34 |
| 67.45±0.45 | 68.18±0.38 | 52.45±1.07 | 73.16±0.78 | 63.9±0.34 | 52.12±0.56 | 49.12±0.46 | 69.12±0.84 | 61.89±0.67 |
| 73.92±0.74 | 75.65±0.47 | 64.37±1.12 | 77.49±0.81 | 72.2±0.34 | 60.22±0.54 | 57.67±0.84 | 71.23±0.34 | 75.90±0.84 |
| 81.94±0.74 | 79.79±0.24 | 80.67±0.84 | 79.23±0.34 | 79.2±0.67 | 70.45±0.32 | 62.96±0.78 | 74.56±0.68 | 79.78±0.22 |
| 85.29±0.22 | 84.49±0.74 | 89.46±0.67 | 81.59±0,54 | 83.19±0.56 | 82.15±0.34 | 71.11±0.68 | 83.89±0.34 | 81.23±0.84 |
| 86.99±0.66 | 86.16±0.84 | 90..79±1.03 | 83.67±0.99 | 87.12±0.45 | 89.12±0.34 | 78.12±0.34 | 87.14±0.78 | 84.45±0.34 |
| 89.55±0.77 | 90.89±0.55 | 90..92±0.54 | 85.99±0.45 | 89.45±0.43 | 91.78±0.45 | 81.99±0.84 | 90.67±0.84 | 86.12±0.68 |
| 90.23±0.67 | 91.78±0.89 | 94.56±0.78 | 89.23±0.86 | 90.12±0.88 | 92.13±0.14 | 86.12±0.22 | 91.23±0.34 | 88.23±0.78 |

**PERCENTAGE RELEASE FROM DIFFERENT FORMULATIONS (F1-F9)**

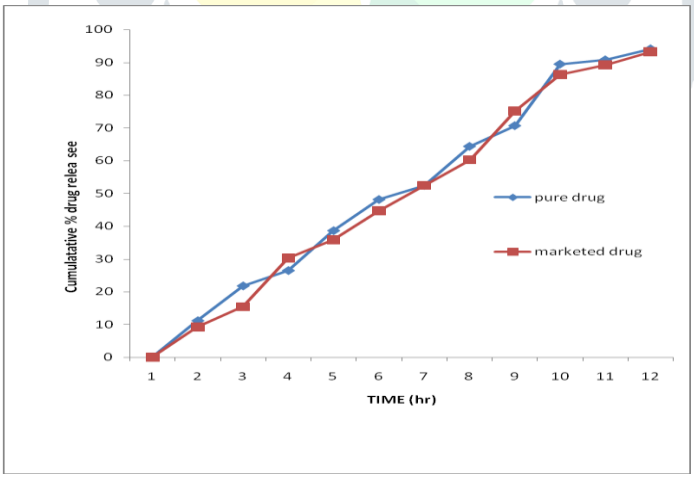
Figure no -8




**FILE OF F3 WITH MARKETED PRODUCT ( table no -5)**

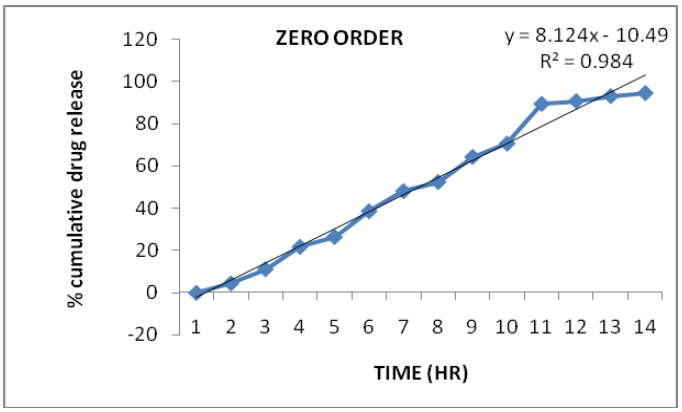
| TIME (HRS) | PURE DRUG | MARKETED DRUG |
|---|---|---|
| 0.5 | 4.49 | 8.45 |
| 1 | 11.19 | 9.23 |
| 2 | 21.79 | 15.45 |
| 3 | 26.48 | 28.23 |
| 4 | 38.64 | 35.86 |
| 5 | 48.16 | 44.67 |
| 6 | 52.45 | 52.42 |
| 7 | 64.37 | 61.23 |
| 8 | 70.67 | 73.14 |
| 9 | 89.46 | 86.23 |
| 10 | 90.78 | 89.23 |
| 11 | 93.12 | 91.23 |
| 12 | 94.56 | 93.24 |

**Different between pure drug &marketed drug (figure no ;9)**

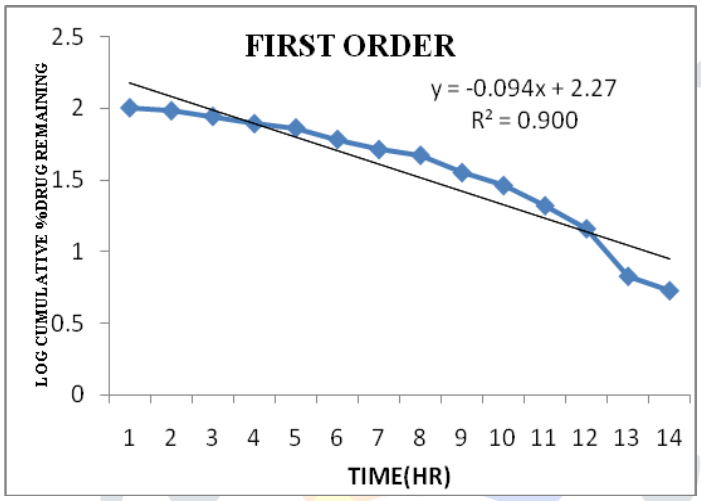



**KINETICS MODELING FOR AN OPTIMIZED FORMULATION (F3)**

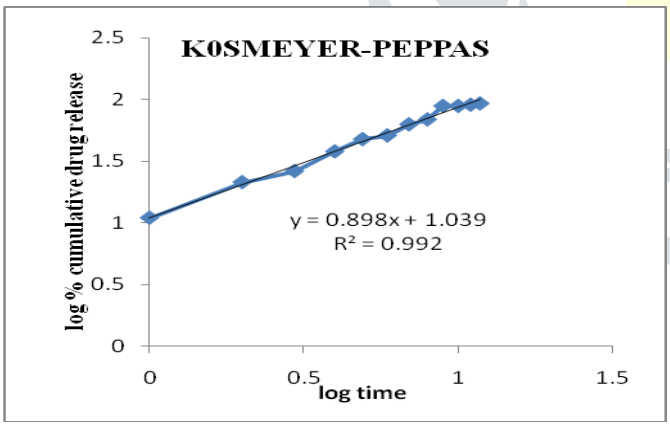
**(Figure no -10)**



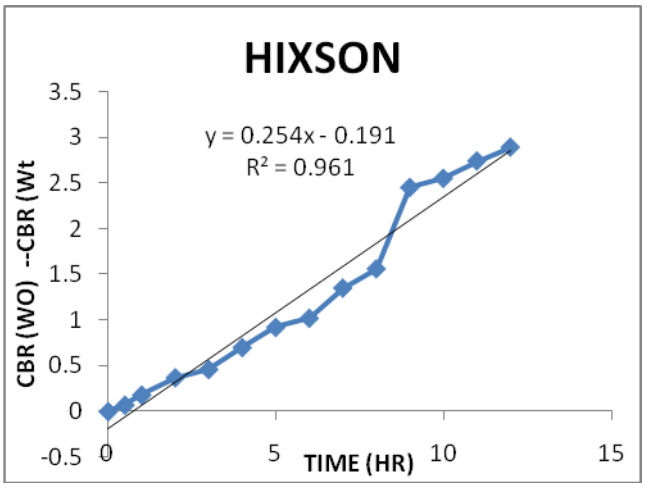

**(Figure no -11)**




**(Figure no -12)**




**(Figure no -13)**




**(Figure no -14)**

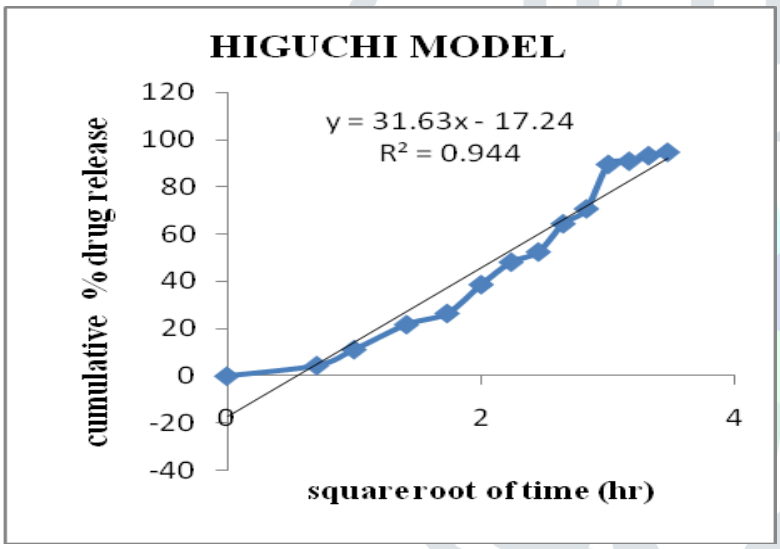



**TABLE NO -6**

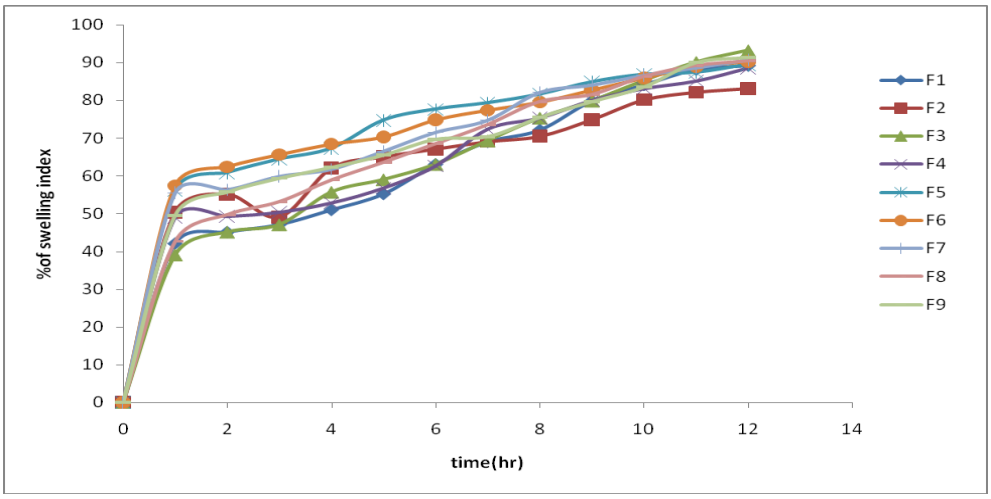
| KINETICS MODEL | R² VALUE |
|---|---|
| ZERO ORDER | 0.984 |
| \ FIRST ORDER | 0.900 |
| HIGUCHI | 0.922 |
| KORSMEYER –PEPPAS | 0.944 |
| HIXSON | 0.961 |

**SWELLING INDEX(%)OF GLIPIZIDE (F1-F9)** TABLE NO-7

| Time (HRS) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 42.09±0.57 | 50.39±0.66 | 39.09±0.46 | 49.04±0.66 | 55.23±0.66 | 57.45±0.46 | 45..54±0.66 | 42.67±0.57 | 49.56±0.46 |
| 2 | 45.12±0.46 | 55.12±0.22 | 45.12±0.66 | 49.27±0.67 | 60.87±0.46 | 62.45±0.46 | 52.37±0.66 | 49.78±0.22 | 55.67±0.66 |
| 3 | 47.12±0.67 | 49.09±0.22 | 47.09±0.67 | 50.36±0.46 | 64.45±0.57 | 65.67±0.46 | 56.89±0.57 | 53.23±0.46 | 59.34±0.57 |
| 4 | 51.01±0.46 | 62.08±0.66 | 55.71±0.57 | 52.84±0.67 | 67.34±0.46 | 68.45±0.57 | 61.78±0.22 | 58.98±0.57 | 62.23±0.46 |
| 5 | 55.23±0.57 | 65.03±0.57 | 59.02±0.22 | 56.78±0.46 | 74.78±0.57 | 70.34±0.22 | 66.56±0.67 | 63.67±0.66 | 65.46±0.57 |
| 6 | 63.05±0.66 | 67.09±0.46 | 63.08±0.66 | 62.64±0.57 | 77.67±0.46 | 74.86±0.46 | 71.56±0.66 | 68.59±0.67 | 69.67±0.34 |
| 7 | 69.05±0.22 | 69.05±0.67 | 69.33±0.67 | 72.39±0.66 | 79.34±0.22 | 77.43±0.22 | 74.78±0.57 | 73.67±0.46 | 70.35±0.66 |
| 8 | 72.16±0.57 | 70.45±0.66 | 75.35±0.57 | 75.34±0.67 | 81.64±0.57 | 79.56±0.46 | 82.15±0.22 | 79.78±0.57 | 75.45±0.57 |
| 9 | 79.88±0.46 | 74.87±0.57 | 79.88±0.66 | 79.99±0.46 | 84.89±0.67 | 82.76±0.57 | 84.09±0.67 | 81.65±0.46 | 79.65±0.46 |
| 10 | 84.14±0.66 | 80.12±0.46 | 85.23±0.46 | 83.13±0.66 | 86.87±0.22 | 85.98±0.66 | 86.67±0.66 | 86.45±0.67 | 83.54±0.46 |
| 11 | 88.19±0.57 | 82.12±0.67 | 90.13±0.57 | 85.13±0.67 | 87.41±0.46 | 88.87±0.57 | 88.67±0.46 | 89.34±0.57 | 89.98±0.66 |
| 12 | 89.23±0.66 | 83.12±0.46 | 93.23±0.22 | 88.56±0.66 | 89.54±0.46 | 90.34±0.46 | 90.78±0.67 | 90.56±0.67 | 91.34±0.22 |

**SWELLING INDEX OF GLIPIZIDE TABLETS AT DIFFERENT TIME INTERVALS**
**(Figure no-15)**




**ACCELERATED STABILITY STUDY OF GLIPIZIDE (TABLET NO – 7)**

| GLPIZIDE TABLET | HARDNESS (kg/cm²) | THICKNESS(mm) | FRIABILITY(%) | DRUG CONTENT UNIFORMITY |
|---|---|---|---|---|
| 1 month | 5.34 | 3.61 | 0.39 | 98.8 |
| 3 months after | 5.26 | 3.56 | 0.39 | 98.3 |

## CONCLUSION

The main aim of this work was to develop MUCOADHESIVE tablets to release the drug at buccal mucosal site in

unidirectional pattern for extended period of time without wash out of drug by saliva. Carbopol, HPMC K4M, and SodiumCMC were selected as MUCOADHESIVE polymers on the basis of their matrix forming properties and Mucoadhesiveness, while ethyl cellulose, being hydrophobic, used as a backing material. Ethyl cellulose has recently been reported to be an excellent backing material, given its low water permeability and moderate flexibility.

**Drug Content and Physical Evaluation:** The assayed drug content in various formulations varied between 94.99% and 103.5% (mean 99.2%). The average weight of the tablet was found to be between 211.9 mg and 214.3mg (mean 213.5 mg), % friability range between 0.31 and 0.42% (mean 0.39 %) and thickness of the tablets for all the formulations was found to be between 3.6 mm and 4.7 mm with average of 4.3 mm. MUCOADHESIVE tablets containing Carbopol showed hardness in the range of 5.3 to 5.7 kg/cm $^2$ and it decreased with increasing amounts of HPMC. The hardness of the tablets containing NaCMC was much lower, ranging from 5.1 to 5.2 kg/cm $^2$ and increased with increasing amounts of HPMC or Carbopol. The difference in the tablet strengths are reported not to affect the release of the drug from hydrophilic matrices. Drug is released by diffusion through the gel layer and/or erosion of this layer and is therefore independent of the dry state of the tablet.

Swelling index was calculated with respect to time. Swelling index increased as the weight gain by the tablets increased proportionally with the rate of hydration as shown in [Table 5- graph no16]. Swelling index measurements could be done upto 12 hours with the tablets containing 150 mg of NaCMC, since it looses its shape at the end of hour. The swelling indices of the tablets with Carbopol and HPMC increased with increasing amounts of Carbopol. Maximum swelling was seen with the formulations (F3, F12, F8, and F1) containing NaCMC and/or Carbopol, the values increased with increasing amounts of NaCMC and/or Carbopol.

*In vitro* drug release studies revealed that the release of Glipizide from different formulations varies with characteristics and composition of matrix forming polymers as shown in tablets no3 to graph no 8. The release rate of Glipizide decreased with increasing concentration of HPMC K4M and CARBOPOL 934 in F3 and F5 to F6 and F8 to F9, respectively. These findings are in compliance with the ability of HPMC to form complex matrix network which leads to delay in release of drug from the device. Carbopol is more hydrophilic than HPMC; it can swell rapidly, therefore decrease of Carbopol content delays the drug release in F3 and F5 to F6. Drug release rate was increased with increasing amount of hydrophilic polymer. The

maximum cumulative percent release of Glipizide from formulation F3 could be attributed due to ionization of Carbopol at pH environment of the dissolution medium.

Table 4 and 5 enlists various dissolution parameters computed for all the controlled release MUCOADHESIVE tablets. To examine further the release mechanism of Glipizide from MUCOADHESIVE tablets, the results were analyzed according to the equation, $Mt/M_{\infty} = Kt^{n}$ proposed by Peppa's and Korsemeye. The obtained values of release rate exponent (n), lie between 0.900 and 0.984 in all formulations for the release of Glipizide. In general, the released pattern found to be non-Fickian tending to approach first order. Several kinetic models describing drug release from immediate and modified released dosage forms. The model that best fits the release data was evaluated by correlation coefficient (r). The correlation coefficient (r) value was used as criteria to choose the best model to describe the drug release from the MUCOADHESIVE tablets. The 'r' value in various models is in table 11. The 'r' values obtained for fitting the drug release data to first order, indicating that the drug release mechanism follows first order kinetics. From higuchi's equation, the high values of correlation coefficient 'r' indicating that the drug release mechanism from these tablets was diffusion controlled. The values of **'n'** in Peppas model indicated the drug release follows non-Fickian diffusion.

From the above results it is concluded that the drug release from the formulated MUCOADHESIVE tablets of Glipizide followed first order kinetics and was diffusion controlled.

,