Formulation Development and Evaluation for Sustained Release Tablet Containing Glibenclamide

Avhad Pratiksha [1*], Dr. Barge Vijaya [2], Dr. Kasabe Amit [3], Deshmane Kamlesh [1], Borase Pallavi [1], Gaikwad Rajratna [1], Pawar Ajay[4]

[1]*Research Scholar, Department of Pharmaceutical Quality Assurance, PDEAs Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre, Pune, Maharashtra, India.*

[2]*Vice Principal, Department of Pharmaceutical Quality Assurance, PDEA'S Shankarrao Ursal College of Pharmaceutical Sciences & Research centre, Kharadi, Pune, Maharashtra, India.*

[3]*Associate Professor, Department of Pharmaceutical Quality Assurance, PDEA'S Shankarrao Ursal College of Pharmaceutical Sciences & Research centre, Kharadi, Pune, Maharashtra, India.*

[4]*Research Scholar, Department of Pharmaceutics, PDEAs Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre, Pune, Maharashtra, India.*

For Correspondence -Avhad Pratiksha B.

pratiavhad9494@gmail.com

ABSTRACT

Objective: The Glibenclamide matrix tablet were prepared using hydrophilic polymers (HPMC complex i.e. HPMC(E4) + calcium phosphate in various proportions as release retarding agent to prolong the drug release and to improve the patience compliance.

Methods: The matrix tablets were prepared by direct compression method. The prepared matrix tablets were subjected to thickness, friability, weight variation test, drug content, hardness, swelling index and in vitro release studies. The drug excipients compatability was evaluated by FTIR studies.

Results: All the formulation showed compliance with pharmacopoeial standards. The in vitro dissolution study shows that F5 formulation was releases the drug in a controlled manner for 12 hours. Among all the formulations, formulation F5 which contains HPMC(E4) calcium complex releases the drugs which follow Zero order kinetics. The FTIR studies was revealed that there was no interaction between drug and excipients.

Conclusion: Hence hydrophilic polymers combination of (HPMC with E4 grade-calcium phosphate complex) in various proportions can be used to prepare matrix tablets of Glibenclamide having prolonged therapeutic effect with enhanced patience compliance.

Keywords: Glibenclamide, HPMC E4-calcium phosphate complex, Sustained release tablet.

INTRODUCTION

Oral sustained release delivery systems are designed to achieve a therapeutically effective concentration of drug in systemic circulation over an extended period of time. Therapeutic benefits of designing SR dosage form include low cost, simple processing, improved efficacy, reduced adverse effects, flexibility in terms of the range of release profiles attainable, increased patient compliance and convenience. Many innovative methods have been developed for obtaining modified drug release. From the practical view point, the least complicated approach for developing a modified release dosage form is the formulation of a hydrophilic matrix tablet [1].

HPMC is the dominant hydrophilic vehicle used for the preparation of oral sustained drug delivery. While HPMC could potentially control the release of a soluble drug, it could also facilitate the release of relatively insoluble drug. In the later case, insolubility of the drug molecule would be the rate limiting step in its release and HPMC's solubilizing effect would facilitate the release. The objective of the present study was to develop a hydrophilic polymer (HPMC – calcium complex) based Glibenclamide matrix sustained release tablet which can release the drug up to time of 12 hours in predetermined rate. The formulation of Glibenclamide matrix tablet was prepared by the polymer combination in order to get required theoretical release profile. The influence of hydrophilic polymer and granulation technique on Glibenclamide was studied. The formulated tablets were also characterized by physical and chemical parameters like drug content, hardness, friability, dissolution rate etc [2].

Diabetes mellitus Type 2 is a long term metabolic disorder that is characterized by high blood sugar, insulin resistance and relative lack of insulin. It primarily occurs due to obesity. Symptoms of high blood sugar include frequent urination, increased thirst and increased hunger [3]. Type 2 diabetes is a progressive condition in which the body becomes resistant to the normal effects of insulin and/or gradually loses the capacity to produce enough insulin in the pancreas. We do not know what causes type 2 diabetes. Type 2 diabetes is associated with modifiable lifestyle risk factors. Type 2 diabetes also has strong genetic and family related risk factors. Type 2

diabetes is diagnosed when the pancreas does not produce enough insulin (reduced insulin production) and/or the insulin does not work effectively and/or the cells of the body do not respond to insulin effectively known as insulin resistance [4]. Over 90% cases of diabetes are type 2 [5,15].

Glibenclamide, also known as Glibenclamide, is an antidiabetic drug belonging to the class of sulfonylureas. Therapy with Glibenclamide is usually initiated with 2.5mg given once daily. The maximal recommended daily dose is 20mg. It has a special status in the treatment of non-insulin-dependent diabetes mellitus because it is effective in many cases which are resistant to all other oral hypoglycemic drugs. It differs from other oral hypoglycemic drugs i.e. more effective during eating than during fasting [6]. It was developed in 1966. It works by binding and inhibiting the ATP-sensitive potassium channels in pancreatic beta cells. It causes cell membrane depolarization, opening voltage-dependent calcium channels. As a result, intracellular calcium level increases in the beta cells and release of insulin is stimulated.

Glibenclamide is a potent sulphonyl urea class which uses an oral hypoglycemic agent. It stimulates insulin release from the beta cells of the pancreas that leads to hypoglycemia. Glibenclamide increases insulin level by reducing the hepatic clearance of the hormone [16]. Glibenclamide belongs to class II (i.e. drugs with low solubility and high permeability) according to the biopharmaceutical classification system [17]. It is practically insoluble in water and consequently, its dissolution has been considered to be the rate-limiting step for absorption. Being weak acid with a pka 5.3, it shows pH dependent solubility and its absorption is expected to be better from the upper part of the gastrointestinal tract (GIT). Plasma half-life of glibenclamide is about 2 to 4 hrs. Various strategies are to be used for the development of oral controlled-release formulations, but the optimum technique should be selected by considering the absorption window of the given drug [5]. The mechanism of action of the drug consists in the inhibition of the ATP-sensitive K+ channels, which leads to depolarization of the cells and insulin secretion[18].

MATERIALS AND METHODS

Material

Glibenclamide was obtained as a sample product from Yarrow chemical products, Mumbai. HPMC E4M was obtained from Ashland Netherlands.co., Magnesium stearate, Talc, Microcrystalline cellulose, was obtained from Research lab Fine chem. Industries, Mumbai. Calcium phosphate was obtained from Yarrow chemical products, Mumbai.

Method

Preparation of HPMC- Calcium Phosphate complex[7]:

- Three biologically relevant calcium phosphates: CaHPO4 ? 2H2O (DCPD), calcium deficient apatite (CDA), and BCP (60% of HA and 40% of b-Ca3(PO4)2) were chosen for the experiments. HPMC (E4M, Dow Chemical), with a molecular weight of 290,000 g/mol, as determined by a laser light diffusion technique, was used.
- One g of each calcium phosphate was mixed with 0.5 g of solid HPMC and 5 mL of doubly distilled water. The mixtures obtained were placed inside glass bottles. The bottles were sealed and kept at 121°C for 48 hours.
- This stage is necessary for simulation of a steam sterilization procedure, widely used in medicine (normally 20 min at 121°C is enough for the sterilization). Later, the bottles were opened and kept for 24 h at 90°C for water evaporation
- No additional treatments were performed with the dry solid composites obtained.
- Chemical and structural analysis of the composites was studied with FTIR (Magna-IR 550, Nicolet) in the range of 400–4000 cm−1 (3–5 mg of the solid composites were mixed with 300 mg of spectral-grade KBr followed by pellet pressing at 12,000 kg/cm2), X-ray diffraction (XRD) (Diffract 5000, Kristalloflex, Siemens) within 2u value of 10–60° (Cu Ka radiation was used), and scanning electron microscopy (SEM) (JSM 6300, JEOL) in the secondary electron mode (acceleration voltage 15 kV).
- Similar measurements were also performed for thermally treated water suspensions of the above calcium phosphates without HPMC (1 g of calcium phosphate and 5 mL of water), and HPMC solution without calcium phosphates (0.5 g of HPMC and 5 mL of water). The latter experiments were used for the control.

- Kristalloflex, Siemens) within 2u value of 10–60° (Cu Ka radiation was used), and scanning electron microscopy (SEM) (JSM 6300, JEOL) in the secondary electron mode (acceleration voltage 15 kV).
- Similar measurements were also performed for thermally treated water suspensions of the above calcium phosphates without HPMC (1 g of calcium phosphate and 5 mL of water), and HPMC solution without calcium phosphates (0.5 g of HPMC and 5 mL of water). The latter experiments were used for the control.

FORMULATION OF SUSTAINED RELEASE TABLET OF GLIBENCLAMIDE

Preparation of Sustained Release Matrix Tablets by Direct Compression Method

Glibenclamide matrix tablets are prepared by direct compression method. The corresponding amount of drug and excipients were accurately weighed and mixedproperly and the matrix is formed. The tablet blends for different batches (F1-F5) areprepared according to Table 1 and further studied for Pre-compression properties.

Table 1: Formulation of Sustain Release Matrix Tablet

Sr. No.	Ingredients	Formulation Codes				
		F1	F2	F3	F4	F5
01	Glibenclamide	5	5	5	5	5
02	HPMC (K4M) complex	50	75	100	125	150
03	Microcrystalline Cellulose	229	204	179	154	129
04	Magnesium Stearate	8	8	8	8	8
05	Talc	8	8	8	8	8
Total		300	300	300	300	300

PRECOMPRESSION EVALUATION OF BLEND OF SUSTAINED RELEASE TABLET OF GLIBENCLAMIDE: [8,9,10,11,12]

Angle of Repose

This is the maximum angle possible between the height of pile of blend powder and horizontal plane. The frictional forces in the lose powder can be measured by angle of repose. The tangent of angle of repose is equal to the coefficient friction (Ɵ) between the particles. Hence the rougher and more irregular the surface of particles the greater will be angle of repose.

$$\Theta = \tan^{-1}(r/h) \qquad \text{.....Eq}^{n}\ (1)$$

Where, H = height of the pile

Table 2: Standards for Angle of Repose

Angle of Repose	Flowability
<20	Excellent
20-30	Good
30-34	passable
>40	Very Poor

Bulk density:

Apparent bulk density (BD) was determined by pouring blend into a graduated cylinder. Weighted quantity of the powder mass (M) was poured into measuring cylinder, then the powder was levelled carefully, and the unsettled apparent volume Vo was noted to the nearest graduated unit. The bulk density was calculated in gm/ml by the formula: The bulk density was calculated using the formula

$$\text{Bulk Density} = M/Vo \qquad \text{----------Eq}^{n}(2)$$

Tapped density: [14]

After determination of the bulk density, the cylinder was tapped mechanically by mounting on a holder in a mechanical tapped density tester that provided a fixed drop of 14 ± 2 mm at a nominal rate of 300 drops per minute. The cylinder was tapped for 500 times initially and the tapped volume Vt was measured to the nearest graduated unit. The tapping was repeated foran additional 750 times and the tapped volume was measured. Final tapped volume was measured and tapped density was calculated by the formula:

Tapped Density = M/Vt. ---------- **Eq^{n} (3)**

Compressibility Index and Hausner's Ratio:

The Compressibility Index and Hausner's Ratio are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of inter-particulate interactions. In a free-flowing powder, such interactions are generallyless significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater inter-particle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the compressibility index or Carr's index (CI) and the Hausner's ratio (HR) which is calculated using the following formulas

Compressibility Index

The simplest way for measurement of free flow of powder is compressibility, a indication of the case with which a material can be induced to how is given by compressibility index (CI) which is calculated as follows

Carr's Index = [(Tapped density - Bulk density)/ Tapped density] ×100 **------(4)**

Table 3: Standards for Compressibility Index

Carr's Index	Properties
5-15	Excellent

Hausner's ratio	Flow
1.2-1.3	Excellent
1.3-1.4	Good
1.4-1.5	Fair
1.5-1.6	Poor
12-16	Good
18-21	Fair to Passable
23-35	Poor
35-38	Very Poor
>40	Very Very Poor

Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by thefollowing formula;

Hausner's ratio (Hr) = [Tapped Density (ρtap)/Bulk Density (ρb)] ------**(5)**

Table 4: Standards for Hausner's Ratio

COMPRESSION OF SUSTAINED RELEASE TABLET OF GLIBENCLAMIDE BY DIRECT COMPRESSION METHOD

Accurate quantity of Glibenclamide and all ingredients were weighed according to formula powders except talc and magnesium stearate was blended homogeneously

in mortar and pestle for 15 minutes. Prepared powder blend was passed through sieve no. 60. Finally, Talc and Magnesium stearate passed from sieve no. 30 added and wasfurther mixed for10 minutes.

Accurately weighed 300 mg homogeneously mixed powder blend was fed manually and compressed with constant compression force and hardness on 16 stations tablet compression machine with 9 mm, breakthrough, and flat faced punches.

Total five formulations were prepared.

EVALUATION OF SUSTAINED RELEASE TABLET OF GLIBENCLAMIDE [8,10,12]

The prepared tablet batches (F1-F5) are subjected to post compression evaluation and evaluation parameters like appearance, weight variation, thickness, hardness, friability, content uniformity, disintegration time, dissolution time was performed and the results are shown in **table 10**.

Appearance:

The tablets were visually observed for capping, chipping and lamination.

Weight Variation:

When a tablet is designed to contain a certain quantity of medication in a specific amount of tablet formula, the weight of the tablet is frequently tested to confirm that the correct amount of drug is included in the tablet. In actuality, ten tablets were consumed and weighed on a digital weighing balance individually.

The average weight of the tablets was determined, and the weight of each tablet was compared to the average. If no more than two tablets are outside the % restriction and no tablet varies by more than twice the percentage limit, the tablet passes the test.

Table 5: Specifications of % weight variation allowed in tablets

Average Weight of Tablet	% Deviation Allowed
80 mg or less	10
More than 80 mg but less than 250 mg	7.5
250 or more	5

Thickness:

The uniformity of tablet size is dependent on the thickness of the tablet. Vernier caliper was used to determine thickness. randomly selected three pills from each formulation were tested to determine it.

Hardness:

The "force necessary to shatter a tablet in diametric compression test" is the definition of hardness. As a result, tablet crushing strength is also known as hardness. The resistancebefore use is determined by the hardness of the material. For each formulation the hardness of 6 tablets was determined using a Pfizer hardness tester. In the hardness tester, tablet was held along its oblong axis in between the two jaws of the tester and the load necessary tocrush it was measured. Then force was applied until the tablet fractured. The value at this point was noted in kg/cm2.

Friability:

This test is used to determine if tablets can survive abrasion while being packed, handled, or transported. Friability is a sign of inadequate tablet ingredient cohesiveness. Friability of the tablets was determined using Roche Friabilator. A total of ten pills are weighed and placed in the Friabilator, which is made up of a circular plastic chamber separated into two or three compartments. The chamber

rotates at 25 revolutions per minute for 4 minutes, dropping the tablets 15 cm away and completing100 rotations. The pills are then weighed for the second time. The weight difference isobserved and given as a percentage difference. It's best if it's less than 1%.

% Friability = (W1-W2)/W1 X 100 ---------- (6)

Where,

W1 = Weight of tablet before test

W2 = Weight of tablet after test

Content uniformity

The Glibenclamide content was estimated as follows.

20 tablets were finely powdered and weight equivalent to 10 mg of Glibenclamide was dissolved in 100 ml of 0.1N HCL and assayed against 0.1 N HCL for drug content using UV-Visible spectrophotometer at 229 nm.

Disintegration test:

Six tablets were placed in each six tubes of the basket and the apparatus operated containing water maintained at 37^0C as the disintegration fluid. The Disintegration time was recorded.

In-vitro Dissolution studies

Dissolution profiles of Glibenclamide tablets were determined using the USP Type II Dissolution test apparatus (paddle) (Electrolab, Mumbai, India). set with a paddle speed of 50 rpm & at temperature 37° C ± 0.5°C. The dissolution media used were 900 mL of 0.1N HCl for first 2 h followed by pH 6.8 phosphate buffer solutions for 12 h. 5 ml samples wereremoved at specified intervals up to 1h and filtered through Whatmann filter paper. An equal volume of fresh medium, prewarmed at 37^0C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Samples were analyzed by UV spectrophotometer at 229 nm. Drug dissolved at specified timeperiods was plotted as cumulative percent release versus time (h) curve.

Stability Study

The prepared sustained release tablet of Glibenclamide were placed in plastic tubes

containing desiccant and stored at ambient conditions, such as room temperature at $40^0C \pm 2^0C$ /75 % RH ± 5% for period of 90 days. Each tablet is weighed and wrapped in aluminum foil and packed in black PVC bottle and put at above specified condition in a heating humidity chamber for 3 months and evaluated for their physical appearance, hardness, disintegrate time, dissolution testing and drug content at specified intervals of time.

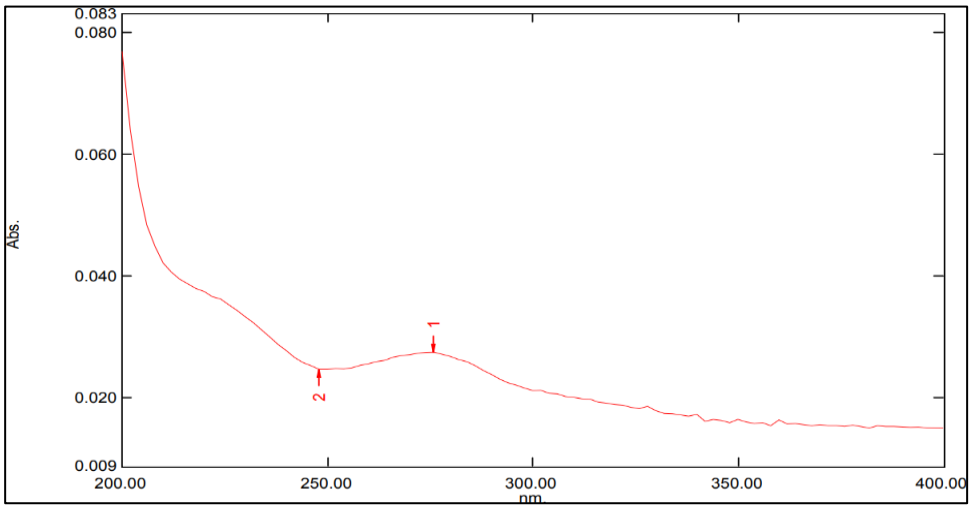
RESULTS AND DISCUSSION

Spectrophotometric Analysis of Glibenclamide UV Spectrophotometric Analysis

Determination of λ max of Glibenclamide in 0.1 N HCL

In UV spectroscopy study, the maximum wavelength (λ max) of Glipizide in 0.1N HCL was found to be 229 nm. The reported λ max value of Glipizide in 0.1N HCL was also 229 nm, so the values similar with the reported value indicates that the given sample of Glibenclamide was in pure form.

Figure 1: UV Spectrum of Glibenclamide in 0.1 N HCl at 229 nm



Preparation of Standard Calibration Curve of Glibenclamide in 0.1N HCl

The Standard curve of Glibenclamide was determined by plotting absorbance Vs concentrationat 229 nm. It was found that there was linear relationship between concentration and absorbance with R^2 value 0.9988. Which reveals that, the drug Glibenclamide obeys the Beers lamberts law.

Table 6: UV Absorbance of Glibenclamide in 0.1 N HCl at 229 nm

Sr.no.	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.028
3	20	0.057
4	30	0.087
5	40	0.121
6	50	0.14

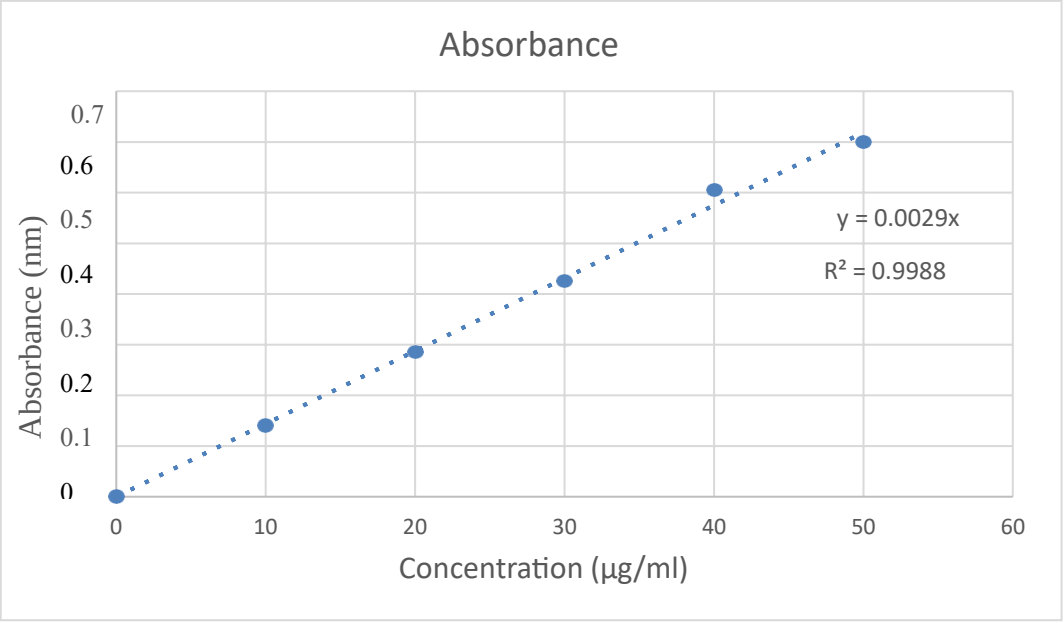


Figure 2: Standard Calibration Curve Graph of Glibenclamide in 0.1N HCL

Determination of λ max of Glibenclamide in 6.8 Phosphate Buffer

In UV spectroscopy study, the maximum wavelength (λ max) of Glibenclamide in 6.8

PhosphateBuffer was found to be 229 nm. The reported λ max value of Glibenclamide in 6.8 Phosphate Buffer was also 229 nm, so the values similar with the reported value indicates that the given sample of Glibenclamide was in pure form.

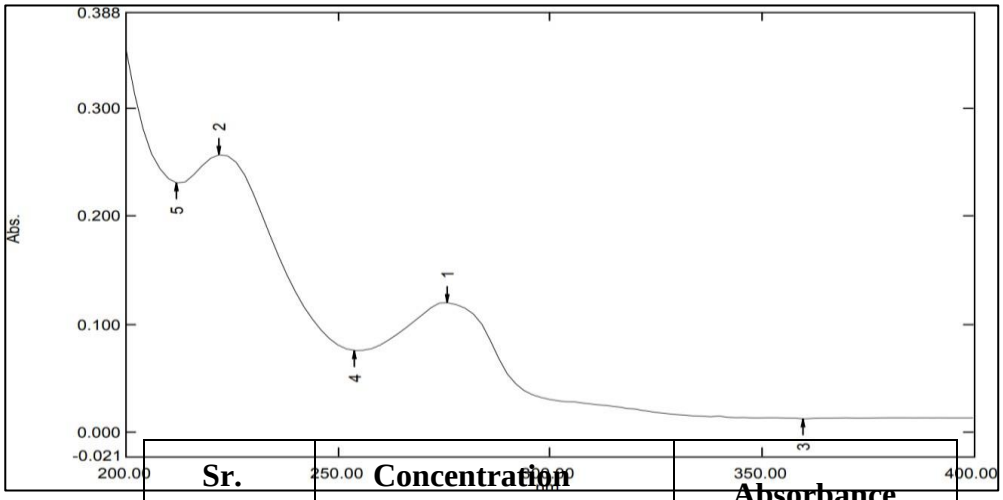


Figure 3: UV Spectrum of Glibenclamide in 6.8 Phosphate Buffer at 229 nm

Sr. no.	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.12
3	20	0.215
4	30	0.315
5	40	0.4
6	50	0.48
7	60	0.6

Table 7: UV Absorbance of Glibenclamide in 6.8 Phosphate Buffer at 229 nm

Preparation of Standard Calibration Curve of Glibenclamide in 6.8 Phosphate Buffer:

The Standard curve of Glibenclamide was determined by plotting absorbance Vs concentration at 229 nm. It was found that there was linear relationship between concentration and absorbance with R2 value 0.9986. Which reveals that, the drug Glibenclamide obeys the Beers lamberts law.

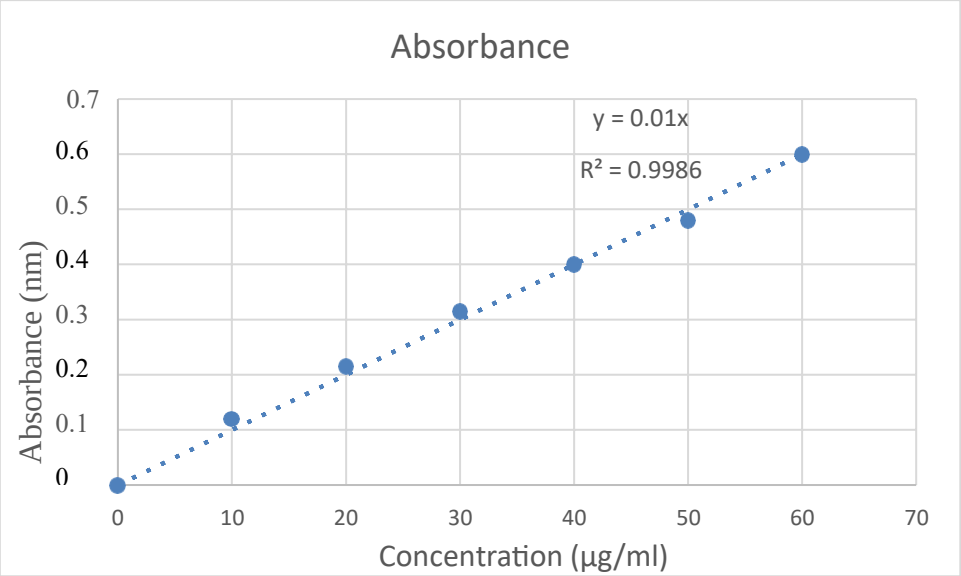


Figure 4: Standard Calibration Curve Graph of Glibenclamide in 6.8 Phosphate Buffer

Drug-Excipient Compatibility Study

Fourier Transform Infra-red Spectroscopy (FTIR) Interpretation of Glibenclamide

The FTIR spectrums of pure Glibenclamide and physical mixtures of drugs and polymers were studied separately as per the excipients used in the formulation. It was observed that there were no major shifts in the main peaks of either drug. This indicates that there were no compatibility problems with the drug with the polymers and excipients used in the formulation. Glibenclamide had peaks at 1658 (C=O amide), 2890 (C=H), 3471 (NH stretch), 1033 (S=O), 1072 (C-O-C).

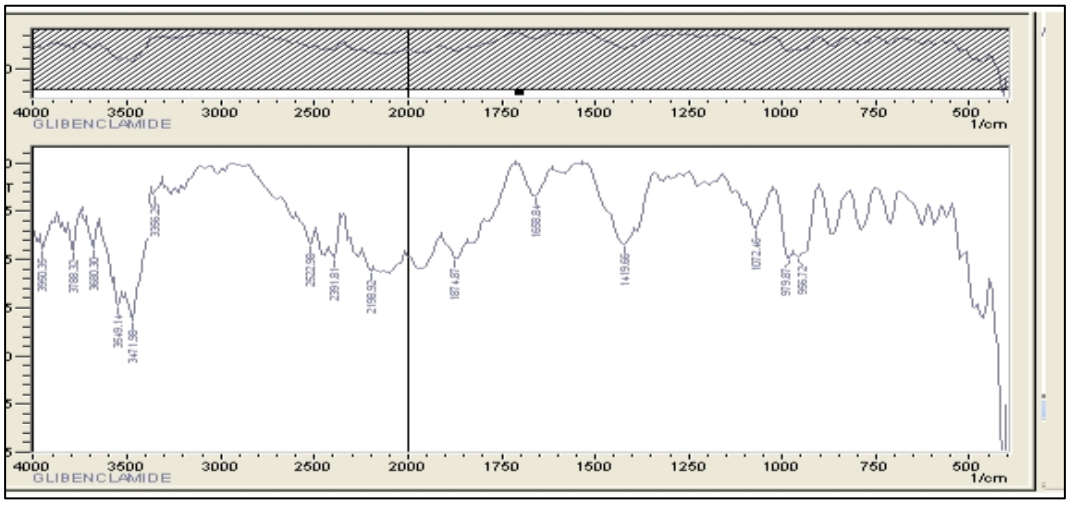


Figure 5: FTIR Spectrum of Glibenclamide

Fourier Transform Infra-red Spectroscopy (FTIR) Interpretation of FTIR of Glibenclamide + HPMC (E4M)- Calcium phosphate (CaPO4) complex

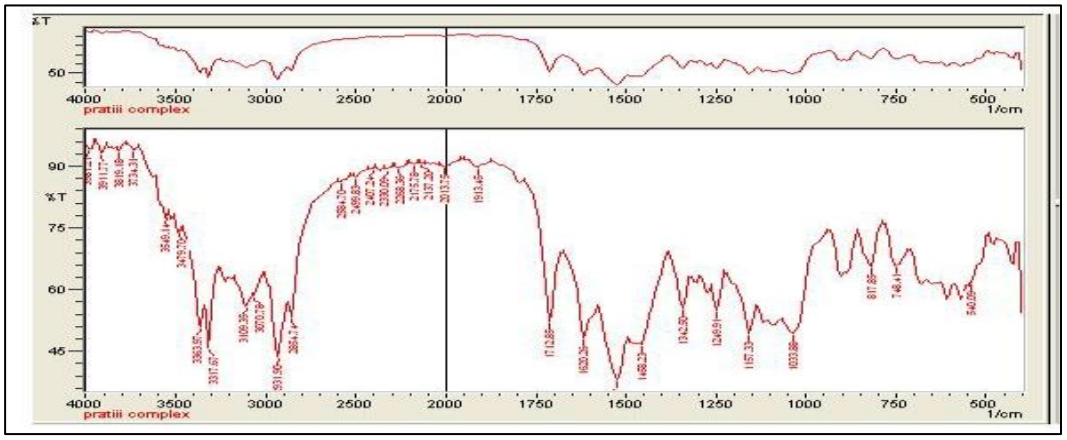


Figure 6: FTIR Graph of Glibenclamide + HPMC (E4M)- Calcium phosphate (CaPO4) complex

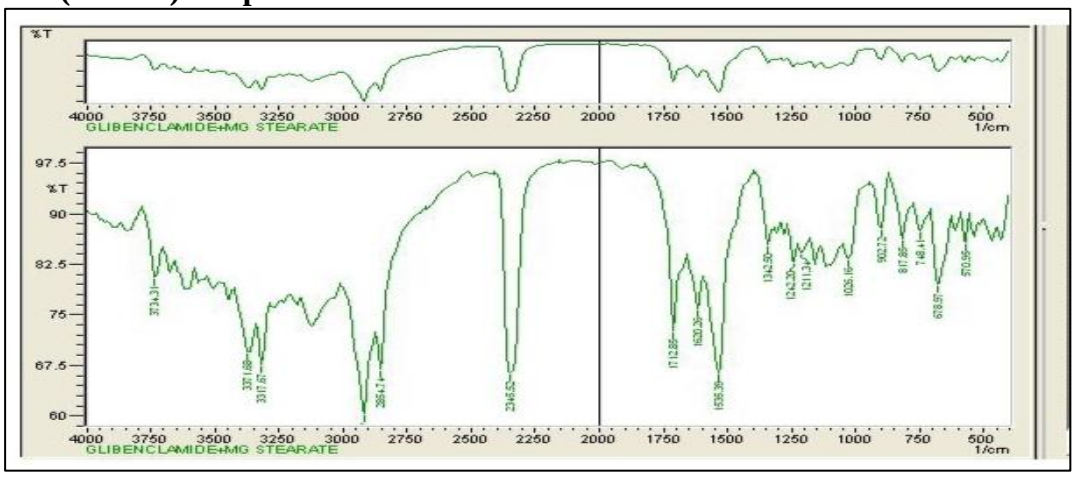


Figure 7: FTIR Graph of Glibenclamide + Mg. Stearate

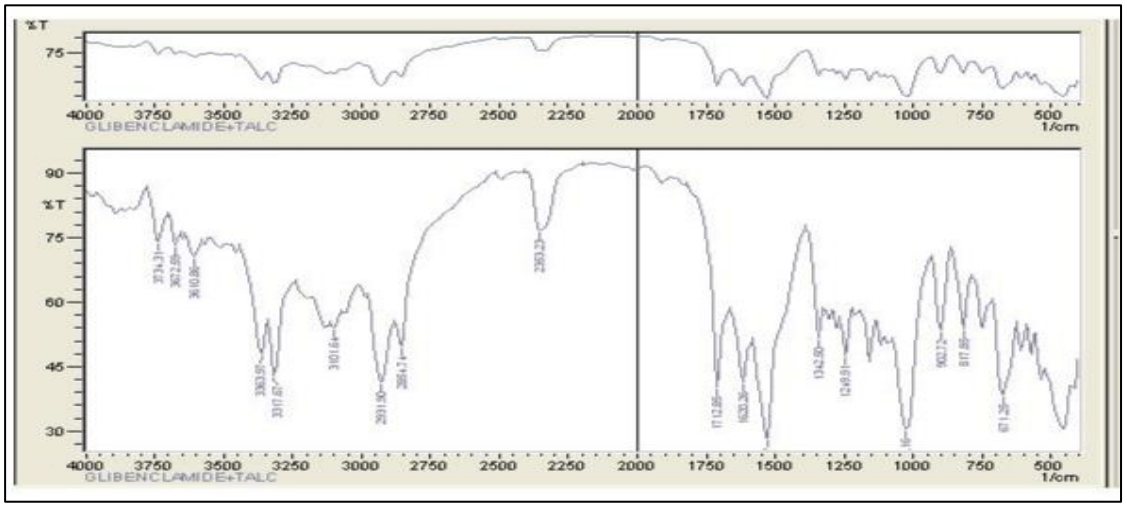


Figure 8: FTIR Graph of Glibenclamide + Talc

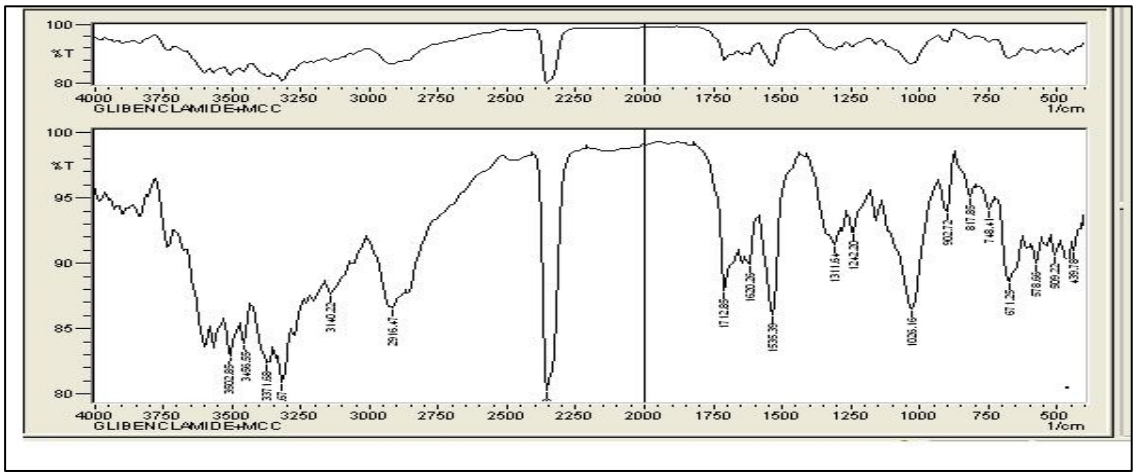


Figure 9: FTIR Graph of Glibenclamide + MCC

PRECOMPRESSION EVALUATION OF BLEND OF SUSTAINED RELEASE TABLET OF GLIBENCLAMIDE:

Sustained release tablets of Glibenclamide were prepared by direct compression method using polymer HPMC-Calcium phosphate complex. A total of five formulations were designed. The flow properties of the powder mixture are important for the uniformity of mass of the tablets; the flow of the powder mixture was analysed before compression to tablets. Low Hausner`s ratio (≤1.18), compressibility index (≤15.68) and angle of repose (≤ 29.39) values indicated fairly good flowability of the powder mixture **Table 8.**

Formulations	Angle of repose (Θ^o)	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Hausner's Ratio (H_R)	Carr's Compressibility index (%)
F1	28.80±0.8	0.42±0.12	0.49±0.23	1.16±0.10	14.28±0.20
F2	28.21±0.5	0.44±0.16	0.51±0.09	1.15±0.21	13.72±0.33
F3	29.24±0.9	0.45±0.40	0.50±0.06	1.11±0.11	10.00±0.52

F4	29.39±0.5	0.41±0.10	0.47±0.20	1.14±0.42	12.76±0.63
F5	28.80±0.8	0.43±0.90	0.51±0.21	1.18±0.36	15.68±0.39

Table 8: Precompression Evaluation of tablet for sustained release tablets

Results are mean of three dimensions*

EVALUATION OF SUSTAINED RELEASE TABLET OF GLIBENCLAMIDE:

As the tablet powder mixture was free flowing, tablets produced were of uniform weight with acceptable weight variation in the range from 298 mg to 301 mg due to uniform die fill. Hardness (5.7 ± 0.5 – 6.1 ± 0.3 kg/cm2) and friability loss (0.71 ± 0.04 - 0.82 ± 0.03 %) indicated that tablets had good mechanical resistance. Drug content was found to be high (≥ 98.75 %) in all the tablet formulations **Table 9 and Table 10.**

Table 9: Evaluation of Sustained Release Tablet of Glibenclamide

Formulations	**Weight variation (mg)**	**Thickness (mm)**	**Hardness (Kg/cm^2)**	**Friability (%)**	**Drug Content (%)**
F1	299±0.50	3.50±0.10	5.7± 0.5	0.78±0.05	95.25
F2	298±0.58	3.40±0.18	5.9± 0.2	0.75±0.06	96.3
F3	301±0.20	3.45±0.25	6.0± 0.3	0.71±0.04	97.9
F4	298±0.85	3.55±0.10	5.8± 0.4	0.82±0.03	98.5
F5	299±0.65	3.48±0.17	6.1± 0.3	0.78±0.07	98.75

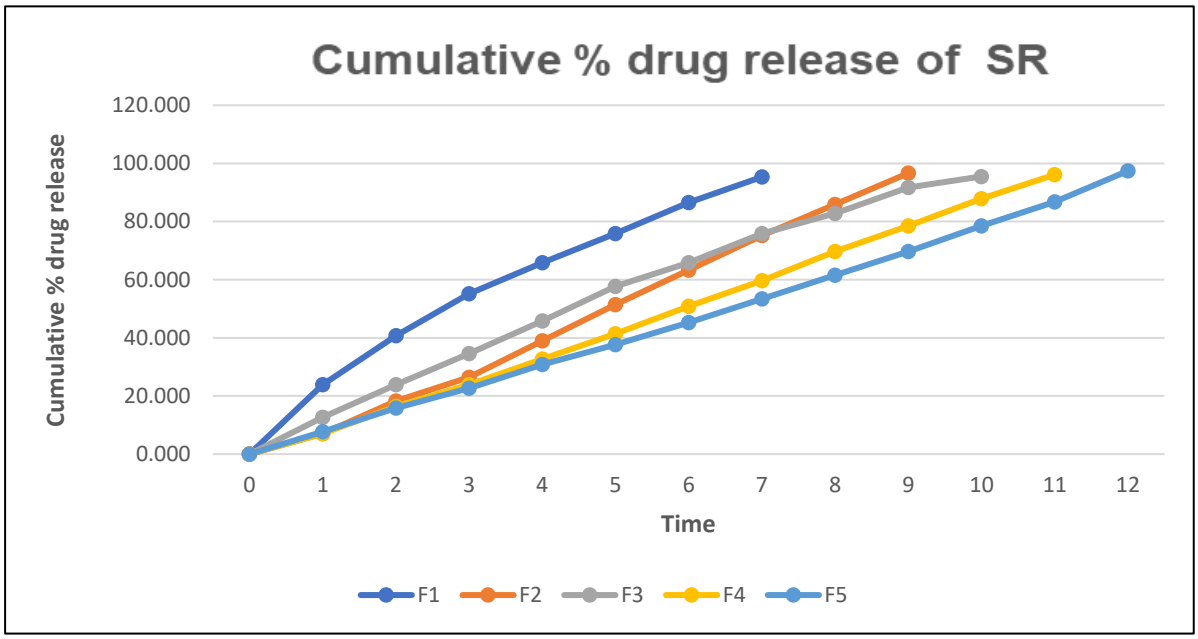
***In vitro* % Drug Release of Drug from Tablet**

All the five tablet batches of fast Sustained release tablet of Glibenclamide were subjected for the in vitro dissolution studies using tablet dissolution test apparatus (USP type II). The

dissolution media used were 900 mL of 0.1 N HCl for first 2 h followed by pH 6.8 phosphate buffersolutions for 12 h.

Table 10: *In vitro* Cumulative % Drug Release from Tablets

Time (Hours)	Cumulative % Drug Release				
	F1	F2	F3	F4	F5
0	0.00	0.00	0.00	0.00	0.00
1	23.99±0.44	7.07±0.48	12.68±0.25	8.94±0.25	9.57±0.55
2	40.76±0.54	18.93±0.52	23.92±0.84	16.43±0.48	15.81±0.35
3	55.15±0.56	33.28±0.85	34.54±0.51	24.56±0.56	22.69±0.65
4	65.80±0.25	47.04±0.55	45.80±0.55	35.80±0.74	31.44±0.26
5	75.85±0.64	58.31±0.84	57.70±0.52	43.95±0.42	40.20±0.45
6	86.53±0.45	68.97±0.52	65.86±0.	53.35±0.57	48.35±0.58
7	95.35±0.48	78.40±0.15	75.91±0.15	61.51±0.65	57.13±0.69
8		86.59±0.45	82.85±0.51	72.18±0.31	65.30±0.22
9		96.66±0.48	91.6±0.45	80.36±0.28	72.85±0.62
10			95.51±0.59	87.93±0.25	81.66±0.44
11				94.88±0.15	89.23±0.64
12					97.43±0.65



STABILITY STUDY

The formulation F5 was selected for stability studies on the basis of their high cumulative % drug release time was studied. The stability studies were carried out at 40˚C±2˚C/75˚C±5% relative humidity for the selected formulation up to two months. For every 1-month time interval the tablets were analysed for drug hardness, content uniformity, % drug release up to two months.

CONCLUSION

In this research work, Preformulation studies of the drug were carried out which includes powder properties and compatibility studies using FTIR. Sustained release tablets were prepared using mixture of hydrophilic polymers such as of HPMC E4M- Calcium phosphate complex. The increasing proportion of polymer in tablet retards the release of drug from tablet. Formulated tablets were evaluated for hardness, friability, thickness, drug content and in-vitro study. F5 batch was selected as optimize batch from the similarity factor, cumulative drug release and drug content study. Then stability study and cumulative release study carried out on optimized batch and compared with marketed product Glynase Xl. Results of present study demonstrated that methodology successfully employed for formulating sustained release matrix tablets of Glibenclamide. The in-vitro dissolution result of batch F5 was fitted best to the kinetic properties as well as showed better similarity to innovator brand Glynase XL (10 mg).

ACKNOWLEDGEMENT

For the completion of the research work the authors would like to show sincere gratitude to PDEA'S Shankarrao Ursal College of Pharmaceutical Sciences & Research center, Kharadi, Pune to provide a lot of support and help whenever needed.

CONFLICT OF INTEREST

All authors declared no conflicts of interest.

REFERENCES

1. Ponchel G, Irache J. Specific and non-specific bioadhesive particulate systems for oral delivery to the gastrointestinal tract. Adv Drug Deliv Rev 1998; 34(2-3): 191-219. http://dx.doi.org/10.1016/S0169-409X(98)00040-4 PMID: 10837678
2. Shree Ram Jayaswal et.al. international journal of pharmacy & technology, Volume 6 Issue 2, Page No. 6527-6586
3. https://en.wikipedia.org/wiki/diabetes_mellitus
4. https://www.diabetesaustralia.com.au/type-2- diabetes
5. Tripathi K.D, Essential's of Pharmacology 7th edition, Page. No.258.
6. Marikanti Rajkumar et.al. J.Chem.Pharm.Res., 2010,2(4):291-303
7. Dorozhkin, S. V. (2000). Is there a chemical interaction between calcium phosphates and hydroxypropylmethylcellulose (HPMC) in organic/inorganic composites? Journal of Biomedical Materials Research, 54(2), 247–255
8. Lieberman H.A., Lachman L., The Theory and Practice of Industrial Pharmacy, Indian Edition, CBS Publishers, and Distributors Pvt. Ltd., 2009, 293, 457, 479-501.
9. Lieberman HA, Lachman L, Schwartz JB. Pharmaceutical dosage forms: Tablets, Ed 3, New York, Marcel Dekker, 1990.225-228.
10. https://go.drugbank.com/drugs/DB01016
11. Michael E Aulton. Pharmaceutics, The Science of Dosage form Design. 2nd Edition. 2005.335-346.
12. Leon Lachman, Herbart liebeman. The theory and practice of industrial pharmacy. Indian Edition CBS publishers.2009.331-334.
13. Won Kyung Kim, et.al., Sustained-Released Formulation of Nifedipine Solid Dispersion with Various Polymers, Macromolecular Research, November 28, 2019.
14. Kuldeep H. Ramteke, et.al., Design, Development and Optimization of Glibenclamide Sustained Release Matrix Tablet by Using Natural Polymers, Current Applied Polymer Science, 2019, 3, 197-211
15. Mellitus D. Diagnosis and classification of diabetes mellitus. Diabetes care. 2005 Jan 1;28(S37): S5-10.

16. Wei H, Löbenberg R. Biorelevant dissolution media as a predictive tool for glyburide a class II drug. Eur J Pharm Sci 2006; 29(1): 45- 52. http://dx.doi.org/10.1016/j.ejps.2006.05.004 PMID: 16815694

17. Löbenberg R, Krämer J, Shah VP, Amidon GL, Dressman JB. Dissolution testing as a prognostic tool for oral drug absorption: dissolution behavior of glibenclamide. Pharm Res 2000; 17(4): 439-44.

18. https://go.drugbank.com › drugs