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ENHANCING ORAL HYPOGLYCEMIC THERAPY: DEVELOPMENT AND EVALUATION OF GLIPIZIDE FLOATING DRUG DELIVERY SYSTEM FOR PROLONGED DRUG RELEASE

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Abstract
Objectives: This study aimed to develop and evaluate a floating drug delivery system for an oral hypoglycemic agent, Glipizide.
Methods: Floating tablets of Glipizide were formulated using HPMC K4M, sodium alginate, and xanthan gum as polymers. Both pre-compression and post-compression evaluations were conducted according to pharmacopoeia standards. The tablets were prepared via direct compression method. Dissolution tests were performed using a USP dissolution testing apparatus II.
Results: FTIR analysis confirmed the compatibility of Glipizide with the selected polymers, indicating no interactions. Release data were analyzed using various models to determine release kinetics and mechanisms, revealing a non-Fickian diffusion mechanism. Increasing polymer concentrations significantly extended the floating lag time.
Interpretation and Conclusion: Dissolution studies indicated that the formulation containing sodium alginate provided superior sustained release. The release kinetics of all formulations adhered to a non-Fickian mechanism. The developed floating tablets of Glipizide demonstrated potential for prolonged drug release up to 12 hours, enhancing bioavailability and patient compliance.

Keywords: Glipizide, gastroretentive, floating drug delivery, sustained release, hypoglycemia.

Introduction

The management of diabetes mellitus heavily relies on oral hypoglycemic agents to control blood glucose levels effectively. Among these agents, Glipizide, a sulfonylurea, is widely used due to its ability to stimulate insulin secretion from the pancreas. Despite its effectiveness, Glipizide's therapeutic potential is often limited by its short half-life and rapid gastrointestinal transit time, which can impede its absorption in the upper gastrointestinal tract. To address these challenges, the development of a floating drug delivery system (FDDS) offers a promising strategy to enhance the bioavailability and prolong the therapeutic effect of Glipizide.
Floating drug delivery systems are designed to remain buoyant in the stomach for extended periods, thereby enhancing gastric retention time and improving drug absorption. This approach is particularly

beneficial for drugs like Glipizide, which are primarily absorbed in the stomach and proximal part of the small intestine. Various studies have demonstrated the effectiveness of FDDS in improving the pharmacokinetic and pharmacodynamic profiles of different drugs [1].

For example, Ramesh Bomma et al. developed floating matrix tablets of norfloxacin using HPMC and xanthan gum, achieving desirable floating properties and sustained drug release over 9 hours [2]. Similarly, Mahesh C et al. formulated gastroretentive dosage forms for ofloxacin, achieving prolonged gastric retention and sustained release using psyllium husk and HPMC [3]. These studies highlight the potential of hydrophilic polymers in achieving desired floating and release characteristics. Further investigations by Sangeka S et al. showed that the presence of food significantly prolongs the gastric retention of floating tablets [4]. Yalçın Özkan et al. found that a 20% HPMC formulation provided optimal release characteristics for diclofenac sodium from HPMC and chitosan matrix tablets [5]. Bodmeier R et al. demonstrated that including polypropylene foam powder in FDDS could enhance buoyancy and sustain drug release for up to 8 hours. optimized a hydrodynamically balanced system for metformin, showing that low-density polymers like HPMC K4M and ethyl cellulose could significantly improve in vitro buoyancy and drug release [6].

Building on this body of research, this study aims to develop and evaluate a floating drug delivery system for the oral hypoglycemic agent Glipizide. By incorporating polymers such as HPMC K4M, sodium alginate, and xanthan gum, the system seeks to achieve prolonged gastric retention, controlled drug release, and improved bioavailability. The present investigation focuses on the formulation and evaluation of Glipizide floating tablets, assessing their pre-compression and post-compression characteristics, dissolution profiles, and release kinetics.

In conclusion, developing a floating drug delivery system for Glipizide holds significant promise for enhancing oral hypoglycemic therapy. By providing a sustained release mechanism, such a system can improve patient compliance and therapeutic outcomes, offering a more effective management strategy for diabetes mellitus. This study aims to build upon existing research to create an optimized formulation that can effectively deliver Glipizide for better diabetes management.

Material and Methods

Drugs and Chemicals

Pharma-grade materials and the highest quality Laboratory Reagents (LR) were utilized for this study. Double distilled water was employed in all experiments. The key materials used include Glipizide, sourced from Spectrum Pharma Labs in Hyderabad. Hydroxypropyl methylcellulose K4M (HPMC K4M) and sodium alginate, both laboratory-grade, were obtained from Spectrum Pharma Labs. Shreeji Chemicals in Mumbai provided xanthan gum and Avicel, while sodium bicarbonate and lactose were procured from S.D. Fine Chemicals, also in Mumbai. Additionally, Shreeji Chemicals supplied magnesium stearate and talc, and hydrochloric acid was obtained from Center Drug House (P) Ltd in Mumbai.

Instruments

Several instruments were employed for the preparation and evaluation of Glipizide tablets. A UV-visible spectrophotometer (Shimadzu Corporation, Japan) and an FTIR spectrophotometer (IR-Affinity-1, Shimadzu, Japan) were used for analytical purposes. Weight measurements were conducted using an electronic balance from Citizen Scales Pvt. Ltd. The pH levels were measured with a digital pH meter from Digisun Electronics, Hyderabad. Bulk density measurements were performed with an apparatus from Biological Museum, Agra. A tablet-punching machine from Shakti, Ahmedabad, and a Roche friabilator from Biological Museum, Agra, facilitated tablet manufacturing. Tablet hardness testing was carried out using a Pfizer hardness tester, while dimensional measurements were done with a digital caliper from Aerospace. Dissolution testing was conducted using a USP dissolution XXIII apparatus from Electrolab TDL-08L. Finally, a hot air oven from Universal was used for various heating and drying processes.

Preformulation studies

It is one of the important prerequisites in development of any drug delivery system. Preformulation

studies of the drug were performed, which included melting point determination, solubility and compatibility studies.

Determination of melting point

Melting point of Glipizide was determined by capillary method. Fine powder of Glipizide was filled in glass capillary tube (previously sealed on one end). The capillary tube is tied to thermometer and placed in oil bath (light paraffin oil bath), the temperature at which it starts to melt was noted.

Determination of λmax of Glipizide using 0.1 N HCL

A solution of Glipizide containing the concentration 10µg/ml was prepared in 0.1 N HCL and UV spectrum was taken. The solution was scanned in the range of 200-400nm.

Standard calibration curve of Glipizide using 0.1 N HCL

100 mg drug was accurately in 100ml volumetric flask. It was dissolved in 0.1N HCL to gives 1000 µg /ml. the standard stock solution stock solution was then serially diluted with 0.1 N HCL to get 1 to 10 µg/ml of Glipizide. The absorbance was measured against 0.1 N HCL as blank at 220 nm using UV spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

Compatibility

Compatibility studies were performed through FTIR spectroscopy. The IR spectrum of pure drug and physical mixture of drug and polymer was studied. The characteristic absorption peaks of Glipizide obtained were obtained at 4000-500cm^{-1}. It has been observed that there is no chemical interaction between Glipizide and polymers used. From the fig no 5.3, 5.4, 5.5, 5.6, & 5.7 it was observed that peak obtained in spectra drug a polymer which show there were no interaction between drug and polymers [8].

Pre-compression evaluation

Angle of Repose

Angle of repose was determined by using funnel method. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured, and angle of repose was calculated using the formula [6].

$$\emptyset = \tan^{-1}\frac{h}{r}$$

Where, θ is the angle of repose, h is height of pile; r is radius of the base of pile.

Angle of Repose (ɵ)	**Flow**
>25	Excellent
25-30	Good
30-40	Passable
<40	Very poor

Bulk Density

Apparent bulk density (ρb) was determined by pouring the blend into a graduated cylinder. The bulk volume (*Vb*) and weight of powder (*M*) was determined. The bulk density was calculated using the formula.

$$\rho b = \frac{m}{Vd}$$

Tapped Density

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (*Vt*) occupied in the cylinder and weight (M) of the blend was measured. The tapped density (*ρb*) was calculated using the following formula.

$$pt = \frac{m}{Vt}$$

Carr's compressibility index

The simplest way of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility. The compressibility index of the granules was determined by Carr's compressibility index, which is calculated by using the following formula.

$$I = \frac{Vo - Vt}{Vo} \times 100$$

% Compressibility	Flow ability
5 – 12	Excellent
12 – 16	Good
18 – 21	Fair Passable
23 – 35	Poor
33 – 38	Very Poor
< 40	Very Very Poor

Hausner ratio

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula. Where ρt is tapped density and ρd is bulk density. Lower Hausner ratio (< 1.25) indicates better flow properties than higher ones (>1.25).

$$\text{Haunser ratio} = \frac{pt}{pd}$$

Preparation of Glipizide floating

Glipizide floating was prepared by direct compression technique using drug and variable concentration of polymers (HPMC K4M, Sodium alginate, Xanthan gum, Sodium Bicarbonate, MCC, Lactose, Mg-sterate, and Talc). The respective powders & optional additives (composition listed in table-5.3) were blended thoroughly with a mortar and pestle. The powder blended was then lubricated with Mg-stearate, purified talc, and then compressed on a tablet-punching machine.

Post-compression evaluation parameters for formulated tablets[9]

a**. Weight variation**

Twenty tablets from each formulation were selected at random and average weight was determined. Then the individual tablets were weighed and were compared with average weight.

b. Hardness

The hardness of the tablet from each formulation was determined using Pfizer hardness tester.

c. Friability

Friability of the tablets was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and

dropping the tablets at a height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were dedusted using a soft muslin cloth and reweighed. The friability (f) is given by the formula.

Friability (f) = $(1 - \frac{W_0}{W}) \times 100$

Where, W_0 is weight of the tablets before the test and W is the weight of the tablet after the test.

d. Thickness and diameter

The thickness and diameter of tablet was carried out using Digital caliper. Five tablets were used for the above test from each batch and results were expressed in millimeter.

e. Drug content

Powder one tablets extraction was carried out using 0.1 N HCL. The concentration was determined spectrophotometrically against appropriate blank. Calculate the content of Glipizide specific absorbance at 220 nm. As given in IP.

f. *In-vitro* buoyancy studies

The in vitro floating behavior of the tablets was studied by placing them in 100 ml beaker 100 ml of 0.1 N HCl (pH 1.2, 37 ^{0}C). The time, tablet required for the emerge on the surface is floating lag time (FLT) or buoyancy lag time (BLT). Moreover, the time tablet constantly float on the surface of the medium is called total floating time (TFT).

g. *In-vitro* dissolution studies

The release rate of Glipizide from floating tablet was determined using the United States Pharmacopoeia (USP) dissolution testing apparatus II. The dissolution test was performed using 900ml of 0.1 N HCL, at 37 ± 0.5^{0}C and 50 rpm. The samples were taken at pre-selected time intervals with replacement of equal volume of dissolution medium [10,11, 12].

RESULTS

Preformulation studies Determination of melting point

The melting point of Glipizide was found to be in range of 197-199 °C.

ESTIMATION OF GLIPIZIDE BY UV SPECTROSCOPY

Determination of lambda max

Fig: 1 UV Spectra of Glipizide at 10µg/ml concentration. Wavelength of maximum absorption in 0.1N HCL solution was found to be 220nm.

Calibration curve

Table 1: Absorbance data for the calibration curve of Glipizide in 0.1N HCL

Sr. No.	Concentration(µg/ml)	Absorbance
1	0	0
2	2	0.07
3	4	0.133
4	6	0.204
5	8	0.270
6	10	0.340

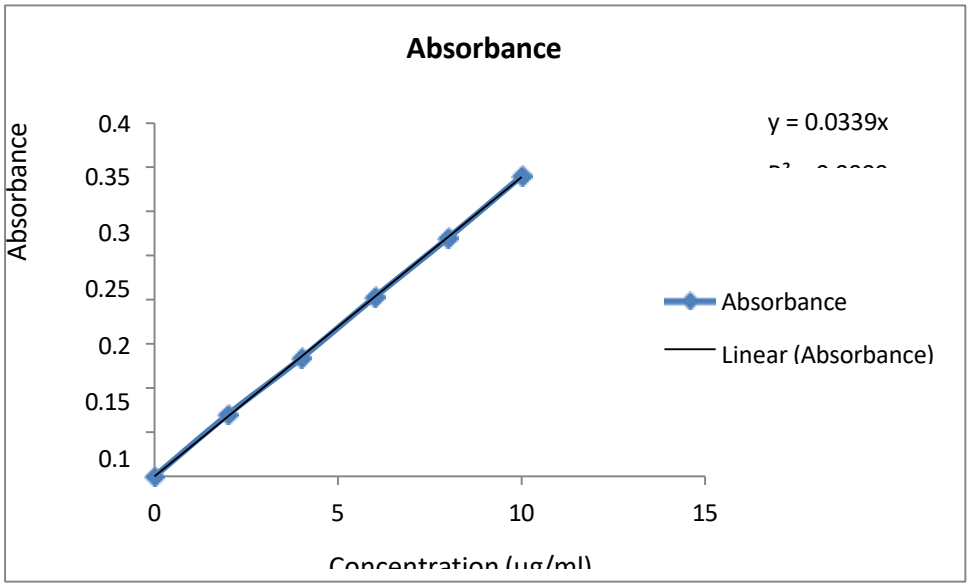
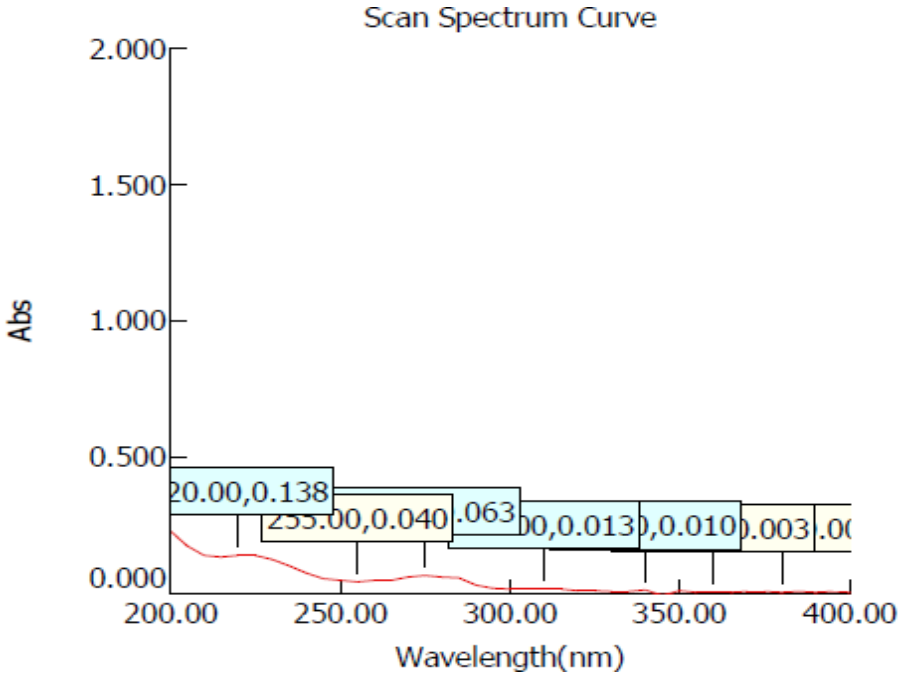


Fig: 2 Standard calibration curve of Glipizide in 0.1N HCl



UV SPECTRUM OF GLIPIZIDE 220nm

COMPATABILITY STUDIES

FTIR Spectroscopy Identification of Glipizide

The IR spectrum of pure drug was found to be similar to the standard spectrum of Glipizide. The spectrum of Glipizide shows the following functional groups at their frequencies shown in table 2

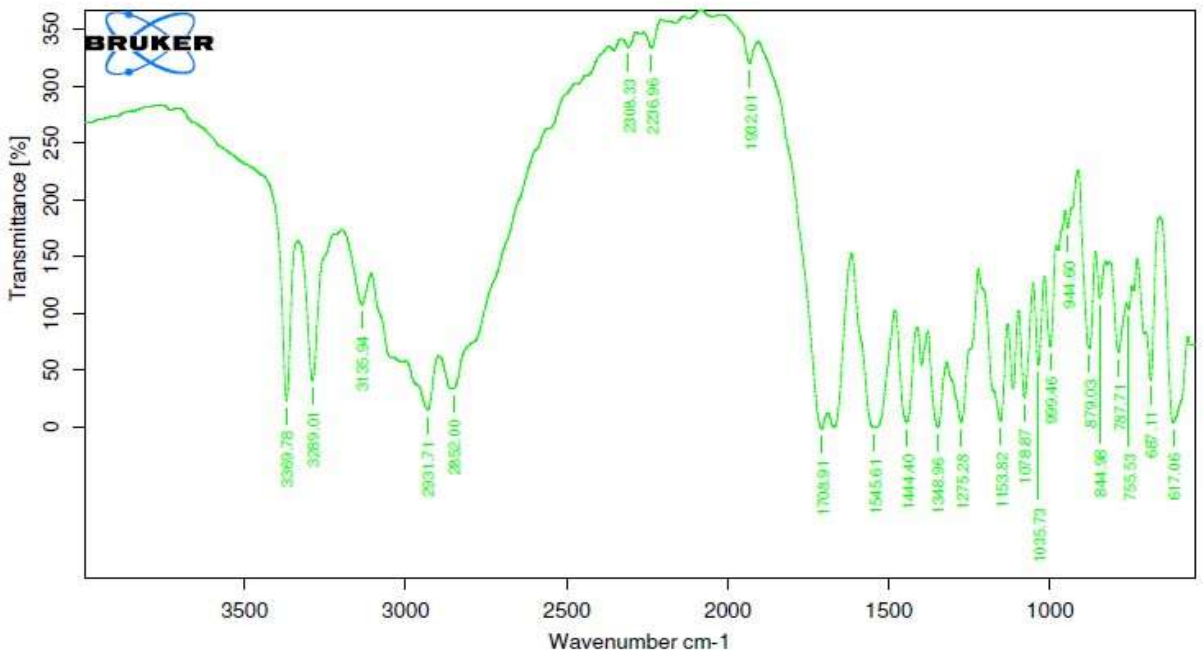


Fig: 3 IR spectra of Glipizide.

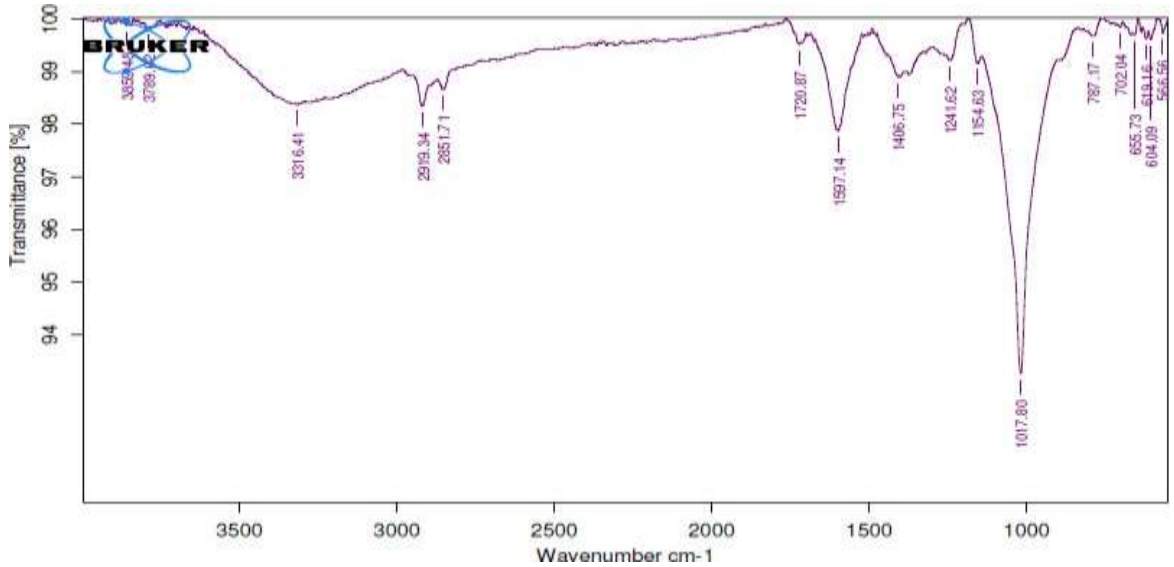


Fig 4: FT-IR Spectra of Xanthan gum

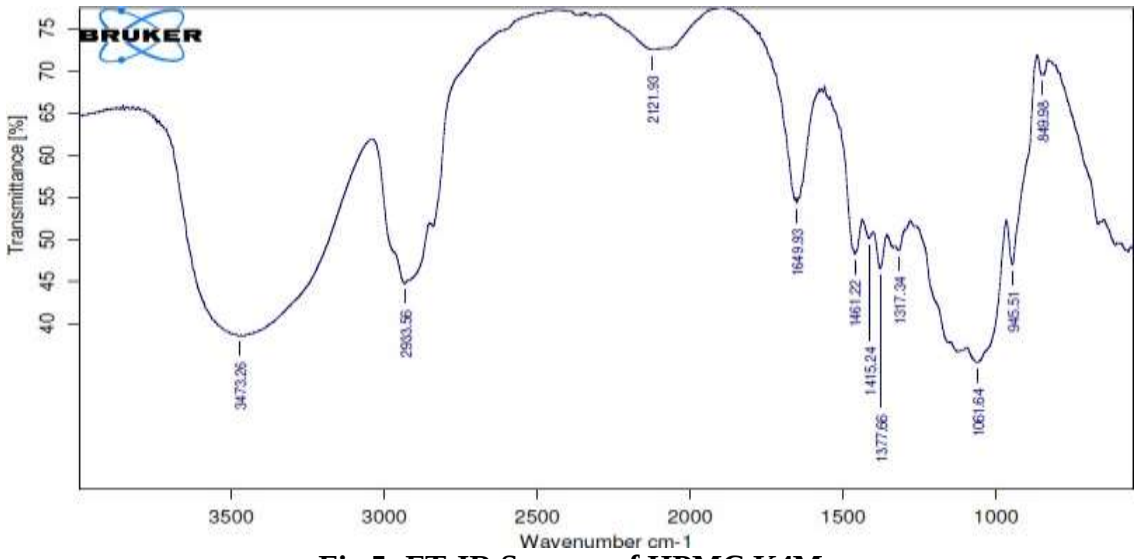
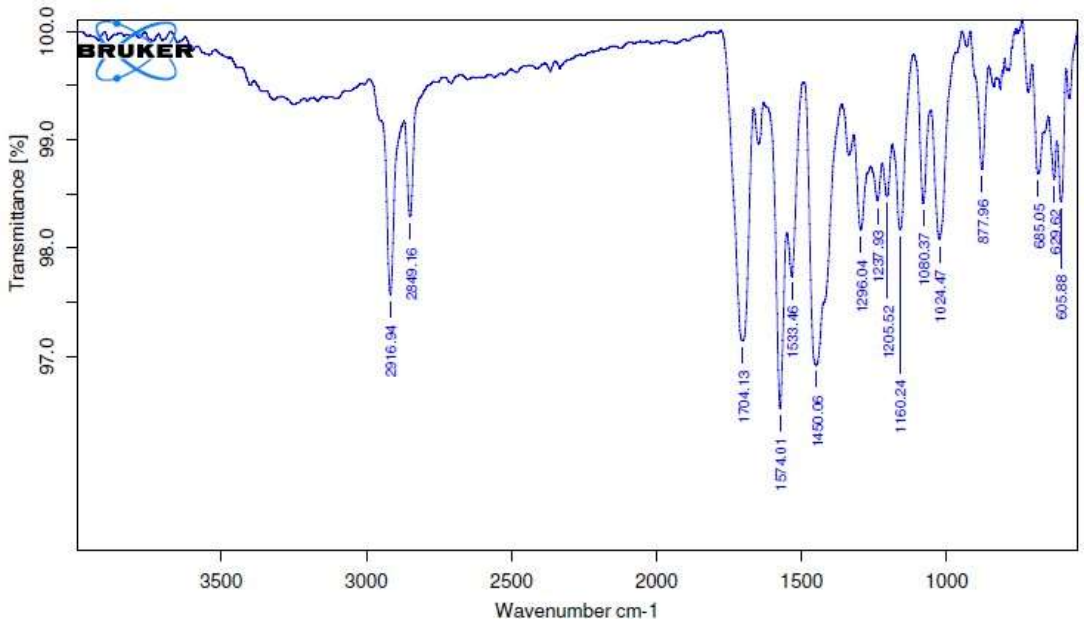


Fig 5: FT-IR Spectra of HPMC K4M

Fig 6: FT-IR Spectra of Sodium alginate



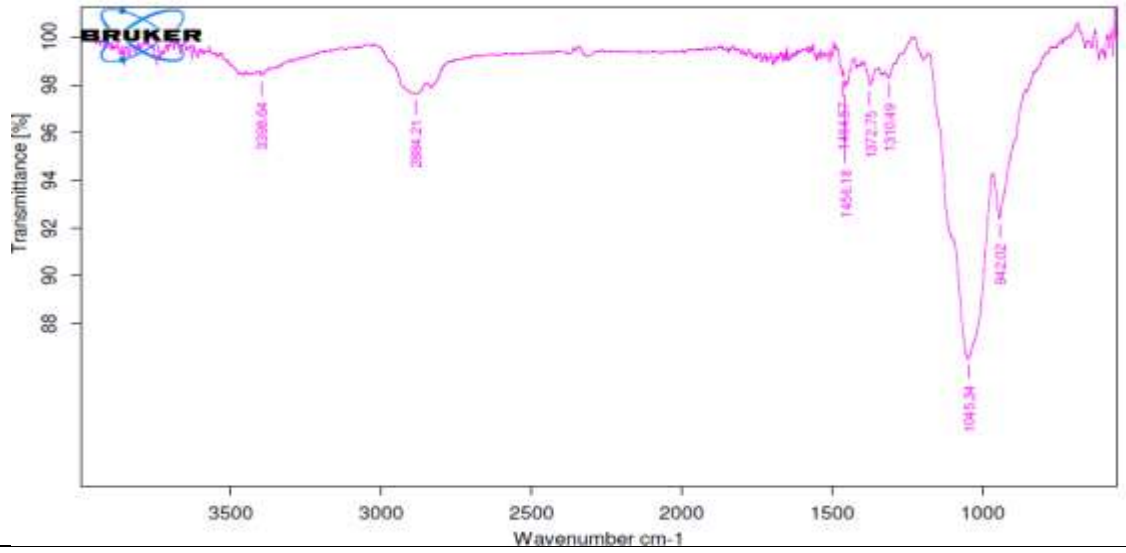


Fig 7:. FT-IR Spectra of Glipizide best formulation.

COMPOSITION OF GLIPIZIDE FLOATING TABLETS

Composition of Glipizide floating tablet with FLT and TLT

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Drug	10	10	10	10	10	10
Sodiumalginate				25	30	35
HPMC K4M	25	30	45			
Xanthan gum	10	15	20	10	15	20
MCC	65	60	50	65	60	60
NAHCO3	20	20	20	20	20	20
MG - STERATE	2	2	2	2	2	2
TALC	3	3	3	3	3	3
LACTOSE	65	60	50	65	60	50
TOTAL WEIGHT	200	200	200	200	200	200
FLT (Seconds)	92	109	133	41	67	87
TFT (h)	>12	>12	12	>12	>12	>12
Ingredients (mg)	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Drug	10	10	10	10	10	10
Sodiumalginate	20	20	20			
HPMC K4M				20	20	20
Xanthan gum	10	15	20	10	15	20
MCC	75	65	70	75	65	70
NAHCO3	20	20	20	20	20	20
MG - STERATE	2	2	2	2	2	2
TALC	3	3	3	3	3	3
LACTOSE	60	65	65	60	65	55
TOTAL WEIGHT	200	200	200	200	200	200
FLT (Seconds)	144	162	187	64	95	107
TFT (h)	>12	>12	12	>12	>12	12

PRE-COMPRESSION EVALUATION OF GLIPIZIDE FLOATING TABLETS

Table 4 pre-compression parameters of Glipizide floating tablets

Formulation code	**Angle of repose (θ) ±SD**	**Bulk density (gm/cm^3) ±SD**	**Tapped density (gm/cm^3) ±SD**	**Hausner ratio (HR)±SD**	**Carr index (Ic) ±SD**

F1	22.43±0.726	0.220±0.010	0.260±0.010	1.180±0.010	15.397±0.594
F2	24.06±0.556	0.225±0.020	0.260±0.010	1.150±0.060	15.792±0.357
F3	22.46±0.471	0.234±0.015	0.270±0.026	1.190±0.010	16.016±0.640
F4	22.64±0.746	0.250±0.010	0.266±0.015	1.124±0.005	11.706±0.512
F5	23.64±0.312	0.230±0.011	0.300±0.010	1.199±0.009	16.676±0.560
F6	22.85±0.665	0.224±0.010	0.262±0.011	1.129±0.006	11.423±0.511
F7	22.21±0.825	0.210±0.010	0.260±0.010	1.180±0.010	15.398±0.594
F8	21.84±0.645	0.230±0.011	0.250±0.010	1.190±0.010	16.015±0.640
F9	21.54±0.346	0.220±0.005	0.282±0.011	1.207±0.004	17.676±0.732
F10	22.87±0.934	0.227±0.010	0.266±0.005	1.173±0.005	15.002±0328.
F11	22.96±0.471	0.230±0.010	0.270±0.010	1.173±0.010	14.827±0.550
F12	22.85±0.520	0.224±0.011	0.260±0.010	1.163±0.030	15.399±0.592

All the values are expressed as mean ± SD. (n=3)

POST COMPRESSION EVALUATION OF GLIPIZIDE FLOATING TABLETS

Table 5: Post-compression evaluation of Glipizide floating tablets

Formulation code	**Weight variation Average wt in (mg)±SD**	**Hardness (Kg/cm^2) ±SD**	**Diameter in (mm) ±SD**	**Thickness in (mm) ±SD**	**Friability (%)±SD**	**Drug content uniformity (%)±SD**
F1	199.58± 0.934	4.355± 0.208	9.34± 0.577	2.245± 0.057	0.756± 0.057	99.672±0.612
F2	200.5± 0.885	4.943± 0.115	9.32± 0.577	2.144± 0.066	0.592± 0.055	97.564±0.407
F3	195.6± 0.824	4.856± 0.115	9.65± 0.577	2.126± 0.055	0.759± 0.015	99.044±0.817
F4	200.04± 0.889	5.062± 0.155	9.00± 0.000	2.250± 0.000	0.671± 0.010	99.486±0.147
F5	200.3±0.833	4.801± 0.200	8.65± 0.577	2.285± 0.057	0.764± 0.011	98.592±0.391
F6	200.2± 0.952	4.932± 0.115	8.67± 0.577	2.129± 0.010	0.766± 0.090	96.362±0.305
F7	199.97± 0.877	4.863± 0.115	9.00± 0.000	2.239± 0.049	0.745± 0.060	98.738±0.228
F8	200.2± 0.834	4.465± 0.115	8.67± 0.577	2.881± 0.052	0.769± 0.011	98.148±0.502
F9	200.15± 0.815	4.737± 0.115	8.65± 0.577	2.942± 0.057	0.663± 0.010	98.424±0.116
F10	200.1± 0.857	4.946± 0.115	8.65± 0.577	2.253± 0.000	0.779± 0.017	98.432±0.355
F11	200.14± 0.815	4.644± 0.115	9.00± 0.000	2.204± 0.100	0.663± 0.010	94.513±0.130
F12	200.12± 0.748	4.802± 0.200	8.67± 0.577	2.355± 0.100	0.782± 0.010	96.172±0.677

All the values are expressed as mean ± SD. (n=3)

IN-VITRO DRUG RELEASE STUDIES

In-vitro drug release data of Glipizide floating tablets

Table 6: *In-vitro* drug release data of Glipizide floating tablets of Batch F1 to F6

	% Cumulative release

Time	FT1±SD	FT2±SD	FT3±SD	FT4±SD	FT5±SD	FT6±SD
1	9.276±0.438	8.000±0.150	7.899±0.88	16.985±0.219	15.052±0.207	10.043±0.174
2	15.478±0.305	15.606±0.306	13.138±0.262	26.900±0.182	24.953±0.218	18.912±0.328
3	18.530±0.133	17.210±0.393	17.629±0.349	29.057±0.304	27.274±0.393	26.637±0.262
4	26.754±0.219	22.358±0.307	16.124±0.231	35.836±0.264	35.117±0.315	36.466±0.267
5	33.838±0.217	26.395±0.353	25.419±0.267	48.825±0.134	44.039±0.353	38.545±0.282
6	35.962±0.278	35.857±0.413	29.327±0.364	53.772±0.349	52.943±0.348	49.082±0.200
7	47.114±0.218	38.709±0.354	35.877±0.308	66.424±0.305	59.637±0.307	59.034±0.307
8	48.987±0.267	45.925±0.365	46.513±0.354	74.421±0.258	68.269±0.309	67.108±0.393
9	59.648±0.183	52.638±0.395	57.518±0.355	75.991±0.524	74.878±0.352	68.340±0.307
10	68.467±0.218	65.236±0.350	62.096±0.269	87.379±0.200	83.945±0.396	77.404±0.256
11	75.267±182	73.736±0.174	69.861±0.267	85.351±0.534	87.733±0.262	83.953±0.958
12	82.346±0.182	78.812±0.135	75.624±0.219	96.083±0.457	91.542±0.782	88.812±0.314

#All the values are expressed as mean ± SD. (n=3)

Table 7: *In-vitro* drug release data of Glipizide floating tablets of

Time	**% Cumulative release**					
	FT7±SD	**FT8±SD**	**FT9±SD**	**FT10±SD**	**FT11±SD**	**FT12±SD**
1	10.831±0.352	8.872±0.172	7.474±0.455	12.323±0.0.447	11.322±0.219	10.625±0.532
2	16.998±0.0.266	11.997±0.328	12.328±0.412	18.331±0.437	15.622±0.397	16.824±0.742
3	24.017±0.352	18.878±0.220	17.341±0.353	28.774±0.744	24.466±0.485	21.058±0.653
4	33.898±0.393	19.618±0.306	21.623±0.307	38.457±0.524	32.158±0.353	27.949±0.698
5	38.828±0.315	23.146±0.399	25.634±0.532	49.716±0.659	43.154±0.439	35.747±0.618
6	45.856±0.353	29.388±0.347	33.853±0.534	58.581±0.656	47.343±0.448	46.248±0.661
7	55.835±0.348	37.172±0.394	39.282±0.332	69.471±0.568	54.060±0.573	55.865±0.662
8	60.689±0.308	44.951±0.353	49.630±0.367	72.428±0.632	64.934±0.513	63.201±0.746
9	67.741±0.352	55.434±0.308	56.568±0.355	78.508±0.228	73.164±0.581	67.382±0.702
10	75.842±0.306	67.828±0.351	64.488±0.397	83.304±0.402	76.211±0.397	73.515±0.747
11	79.132±0.353	74.582±0.308	75.404±0.315	87.488±0.444	82.343±0.415	78.396±0.704
12	88.621±0.414	82.356±0.306	79.521±0.423	92.354±0.864	85.624±0.367	83.731±0.537

Batch F7 to F12

All the values are expressed as mean ± SD. (n=3)

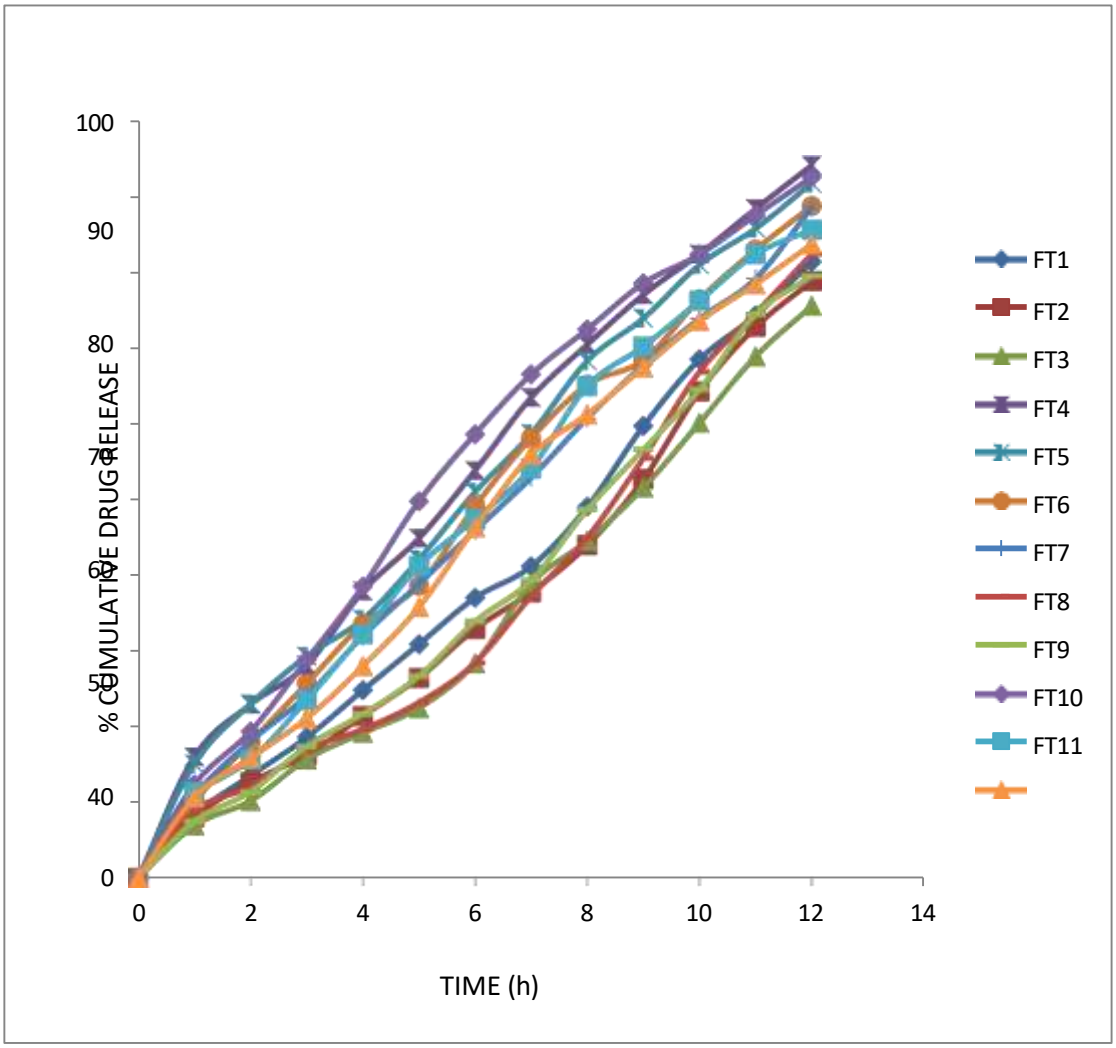


Fig: 9 *In-vitro* drug release profile of Glipizide floating tablets of batches F1 to F12.

DRUG RELEASE KINETICS OF GLIPIZIDE

Zero order release kinetics

Table 8: Zero order kinetics data of Glipizide floating tablets of Batch F1 to F6

Time	% Cumulative release					
	FT1±SD	**FT2±SD**	**FT3±SD**	**FT4±SD**	**FT5±SD**	**FT6±SD**
1	9.272±0.438	8.000±0.150	7.899±0.88	16.985±0.219	15.052±0.207	10.043±0.174
2	15.478±0.305	14.604±0.306	13.138±0.262	26.900±0.182	24.953±0.218	18.912±0.328
3	17.530±0.133	17.210±0.393	16.629±0.349	28.057±0.304	27.274±0.393	26.637±0.262
4	26.754±0.219	23.358±0.307	16.124±0.231	35.836±0.264	34.117±0.315	35.466±0.267
5	33.838±0.217	26.395±0.353	23.419±0.267	48.825±0.134	44.039±0.353	38.545±0.282
6	35.962±0.278	35.857±0.413	29.327±0.364	53.772±0.349	52.943±0.348	49.082±0.200
7	46.114±0.218	39.708±0.354	35.877±0.308	65.424±0.305	57.637±0.307	58.034±0.307
8	47.987±0.267	45.925±0.365	45.513±0.354	74.421±0.258	68.269±0.309	67.108±0.393
9	59.648±0.183	52.638±0.395	57.518±0.355	75.991±0.524	74.878±0.352	68.340±0.307
10	69.467±0.218	65.236±0.350	62.096±0.269	86.379±0.200	83.945±0.396	79.404±0.256
11	75.267±182	72.736±0.174	67.861±0.267	85.351±0.534	87.733±0.262	83.953±0.958
12	82.356±0.182	79.812±0.135	75.624±0.219	95.083±0.457	91.542±0.782	88.812±0.314

#All values are expressed as mean ±SD. (n=3)

Table 9 Zero order kinetics data of Glipizide floating tablets of Batch F7 to F12

Time	% Cumulative release					
	FT7±SD	**FT8±SD**	**FT9±SD**	**FT10±SD**	**FT11±SD**	**FT12±SD**
1	10.831±0.352	8.872±0.172	7.474±0.455	12.323±0.0.447	11.322±0.219	10.625±0.532
2	17.998±0.0.266	11.997±0.328	11.328±0.412	19.331±0.437	15.622±0.397	15.824±0.742
3	24.017±0.352	16.878±0.220	17.341±0.353	28.774±0.744	23.466±0.485	21.058±0.653
4	31.898±0.393	19.618±0.306	21.623±0.307	38.457±0.524	32.158±0.353	27.949±0.698
5	38.828±0.315	23.146±0.399	26.634±0.532	49.716±0.659	41.154±0.439	35.747±0.618
6	45.856±0.353	28.388±0.347	33.853±0.534	58.581±0.656	47.343±0.448	46.248±0.661
7	52.835±0.348	37.172±0.394	39.282±0.332	66.471±0.568	54.060±0.573	55.865±0.662
8	60.689±0.308	44.951±0.353	48.630±0.367	72.428±0.632	64.934±0.513	61.201±0.746
9	67.741±0.352	55.434±0.308	56.568±0.355	78.508±0.228	70.164±0.581	67.382±0.702
10	73.842±0.306	66.828±0.351	64.488±0.397	82.304±0.402	76.211±0.397	73.515±0.747
11	79.132±0.353	74.582±0.308	74.404±0.315	87.488±0.444	82.343±0.415	78.396±0.704
12	88.621±0.414	82.356±0.306	79.521±0.423	92.354±0.864	85.624±0.367	83.731±0.537

#All values are expressed as mean ±SD. (n=3)

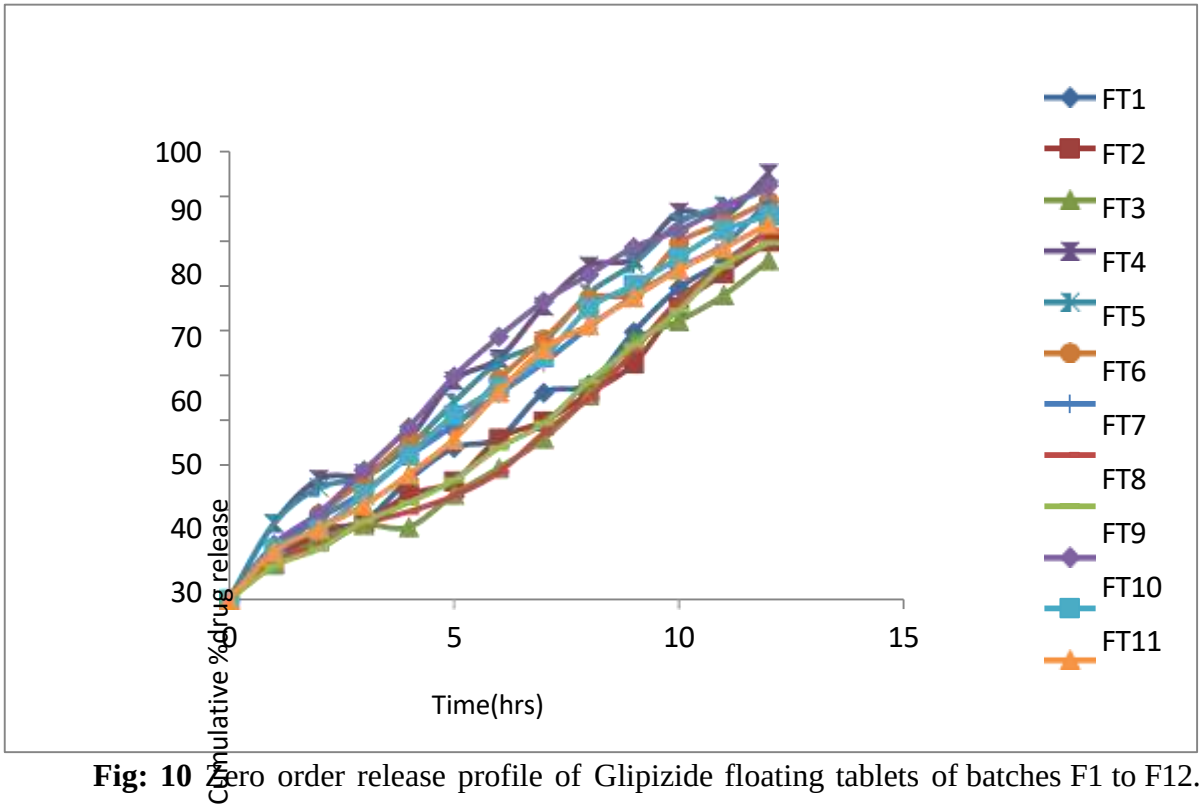


Fig: 10 Zero order release profile of Glipizide floating tablets of batches F1 to F12.

First order release kinetics data of Glipizide floating tablets

Table 10: First order release kinetics of Glipizide of Batch F1 to F6

Time	Log % Cumulative release					
	FT1±SD	**FT2±SD**	**FT3±SD**	**FT4±SD**	**FT5±SD**	**FT6±SD**
1	1.961	1.964	1.969	1.928	1.928	1.948
2	1.943	1.947	1.949	1.893	1.893	1.918
3	1.917	1.929	1.932	1.850	1.856	1.876
4	1.883	1.902	1.914	1.800	1.813	1.828
5	1.847	1.860	1.896	1.748	1.756	1.782
6	1.805	1.834	1.862	1.675	1.690	1.716
7	1.763	1.788	1.794	1.575	1.606	1.634
8	1.698	1.740	1.752	1.486	1.488	1.555
9	1.617	1.667	1.695	1.380	1.434	1.487
10	1.513	1.566	1.612	1.220	1.303	1.390
11	1.394	1.452	1.508	1.028	1.123	1.257
12	1.270	1.327	1.390	0.772	0.915	1.053

Table 11: First order release kinetics of Glipizide of Batch F7 to F12

Time	Log % Cumulative release to remain to release					
	FT7±SD	**FT8±SD**	**FT9±SD**	**FT10±SD**	**FT11±SD**	**FT12±SD**
1	1.950	1.958	1.967	1.94306	1.949	1.952
2	1.918	1.948	1.943	1.912048	1.922	1.930
3	1.887	1.925	1.913	1.858699	1.879	1.903
4	1.838	1.910	1.889	1.796186	1.826	1.864
5	1.792	1.892	1.858	1.70999	1.777	1.815

6	1.742	1.862	1.814	1.622065	1.728	1.739
7	1.683	1.806	1.775	1.538188	1.653	1.655
8	1.606	1.749	1.703	1.455955	1.558	1.598
9	1.522	1.659	1.628	1.352002	1.488	1.527
10	1.434	1.534	1.538	1.271722	1.395	1.438
11	1.338	1.422	1.425	1.13067	1.248	1.314
12	1.058	1.246	1.313	0.864959	1.150	1.210

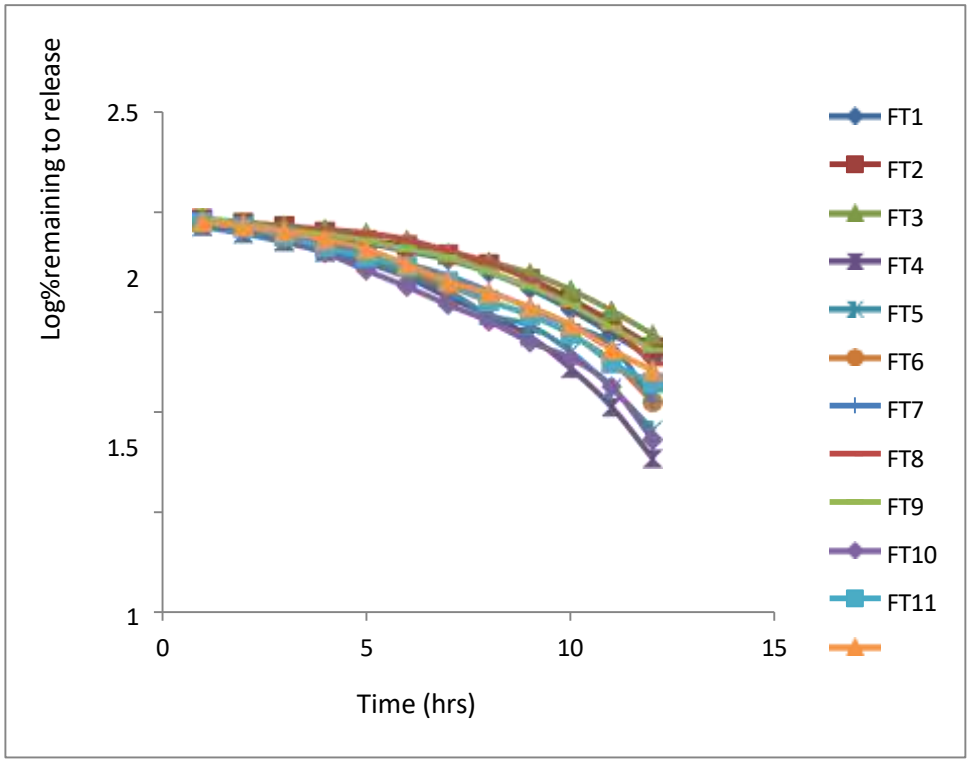


Fig: 11 First order release profile of Glipizide floating tablets of batches F1 to F12.

HIGUCHI RELEASE KINETICS DATA OF GLIPIZIDE FLOATING TABLETS

Table 12 Higuchi release kinetics data of Glipizide of Batch F1 to F6

Root Time	**% Cumulative release**					
	FT1±SD	**FT2±SD**	**FT3±SD**	**FT4±SD**	**FT5±SD**	**FT6±SD**
1.00	9.272±0.438	8.000±0.150	7.899±0.88	16.985±0.219	15.052±0.207	10.043±0.174
1.41	15.478±0.305	14.604±0.306	13.138±0.262	26.900±0.182	24.953±0.218	18.912±0.328
1.73	17.530±0.133	17.210±0.393	16.629±0.349	28.057±0.304	27.274±0.393	26.637±0.262
2.00	26.754±0.219	23.358±0.307	16.124±0.231	35.836±0.264	34.117±0.315	35.466±0.267
2.23	33.838±0.217	26.395±0.353	23.419±0.267	48.825±0.134	44.039±0.353	38.545±0.282
2.44	35.962±0.278	35.857±0.413	29.327±0.364	53.772±0.349	52.943±0.348	49.082±0.200

2.64	46.114±0.218	39.708±0.354	35.877±0.308	65.424±0.305	57.637±0.307	58.034±0.307
2.82	47.987±0.267	45.925±0.365	45.513±0.354	74.421±0.258	68.269±0.309	67.108±0.393
3.00	59.648±0.183	52.638±0.395	57.518±0.355	75.991±0.524	74.878±0.352	68.340±0.307
3.16	69.467±0.218	65.236±0.350	62.096±0.269	86.379±0.200	83.945±0.396	79.404±0.256
3.31	75.267±182	72.736±0.174	67.861±0.267	85.351±0.534	87.733±0.262	83.953±0.958
3.46	82.356±0.182	79.812±0.135	75.624±0.219	95.083±0.457	91.542±0.782	88.812±0.314

#All values are expressed as mean ±SD. (n=3)

Table 13 Higuchi release kinetics data of Glipizide of Batch F7 to F12

Root	**% Cumulative release to remain to release**					
Time	**FT7±SD**	**FT8±SD**	**FT9±SD**	**FT10±SD**	**FT11±SD**	**FT12±SD**
1.00	10.831±0.352	8.872±0.172	7.474±0.455	12.323±0.447	11.322±0.219	10.625±0.532
1.41	17.998±0.0.266	11.997±0.328	11.328±0.412	19.331±0.437	15.622±0.397	15.824±0.742
1.73	24.017±0.352	16.878±0.220	17.341±0.353	28.774±0.744	23.466±0.485	21.058±0.653
2.00	31.898±0.393	19.618±0.306	21.623±0.307	38.457±0.524	32.158±0.353	27.949±0.698
2.23	38.828±0.315	23.146±0.399	26.634±0.532	49.716±0.659	41.154±0.439	35.747±0.618
2.44	45.856±0.353	28.388±0.347	33.853±0.534	58.581±0.656	47.343±0.448	46.248±0.661
2.64	52.835±0.348	37.172±0.394	39.282±0.332	66.471±0.568	54.060±0.573	55.865±0.662
2.82	60.689±0.308	44.951±0.353	48.630±0.367	72.428±0.632	64.934±0.513	61.201±0.746
3.00	67.741±0.352	55.434±0.308	56.568±0.355	78.508±0.228	70.164±0.581	67.382±0.702
3.16	73.842±0.306	66.828±0.351	64.488±0.397	82.304±0.402	76.211±0.397	73.515±0.747
3.31	79.132±0.353	74.582±0.308	74.404±0.315	87.488±0.444	82.343±0.415	78.396±0.704

3.46	88.621±0.414	82.356±0.306	79.521±0.423	92.354±0.864	85.624±0.367	83.731±0.537

#All values are expressed as mean ±SD. (n=3)

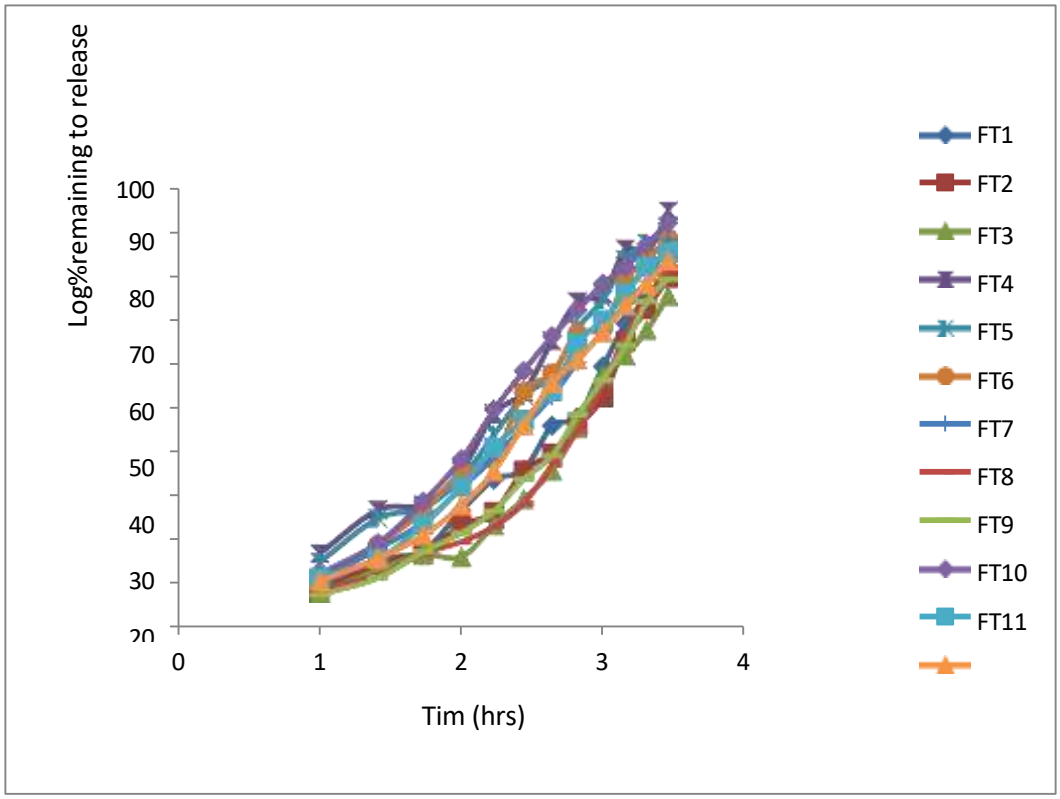


Fig: 12 Higuchi release kinetics profile of Glipizide floating tablets of batches F1 to F12.

Table 14 Peppas release kinetics data of Glipizide floating tablets of Batch F1 to F6

Log Time	**Log % Cumulative release**					
	FT1±SD	**FT2±SD**	**FT3±SD**	**FT4±SD**	**FT5±SD**	**FT6±SD**
0.00	0.916	0.904	0.843	1.176	1.178	1.042
0.301	1.094	1.063	1.047	1.340	1.342	1.229
0.477	1.242	1.183	1.166	1.462	1.452	1.392
0.602	1.374	1.309	1.259	1.567	1.544	1.512
0.698	1.474	1.438	1.330	1.642	1.634	1.598
0.778	1.553	1.504	1.437	1.723	1.706	1.682
0.845	1.623	1.588	1.579	1.796	1.774	1.757
0.903	1.697	1.653	1.637	1.842	1.840	1.807

0.954	1.769	1.728	1.702	1.880	1.861	1.840
1.00	1.828	1.800	1.772	1.922	1.903	1.878
1.041	1.877	1.854	1.832	1.952	1.937	1.914
1.079	1.910	1.897	1.878	1.974	1.963	1.948

Table 15 Peppas release kinetics data of Glipizide floating tablets of Batch F7 to F12

Log Time	**Log % Cumulative release to remain to release**					
	FT7±SD	**FT8±SD**	**FT9±SD**	**FT10±SD**	**FT11±SD**	**FT12±SD**
0.00	1.034	0.948	0.874	1.088	1.050	1.024
0.301	1.230	1.042	1.090	1.264	1.221	1.170
0.477	1.363	1.042	1.264	1.444	1.389	1.303
0.602	1.488	1.268	1.355	1.574	1.520	1.432
0.698	1.578	1.346	1.442	1.688	1.604	1.540
0.778	1.652	1.438	1.543	1.760	1.666	1.656
0.845	1.715	1.559	1.604	1.817	1.740	1.738
0.903	1.776	1.643	1.696	1.854	1.806	1.778
0.954	1.825	1.734	1.760	1.888	1.838	1.823
1.00	1.863	1.819	1.817	1.912	1.877	1.860
1.041	1.893	1.867	1.866	1.937	1.916	1.898
1.079	1.948	1.916	1.900	1.967	1.934	1.924

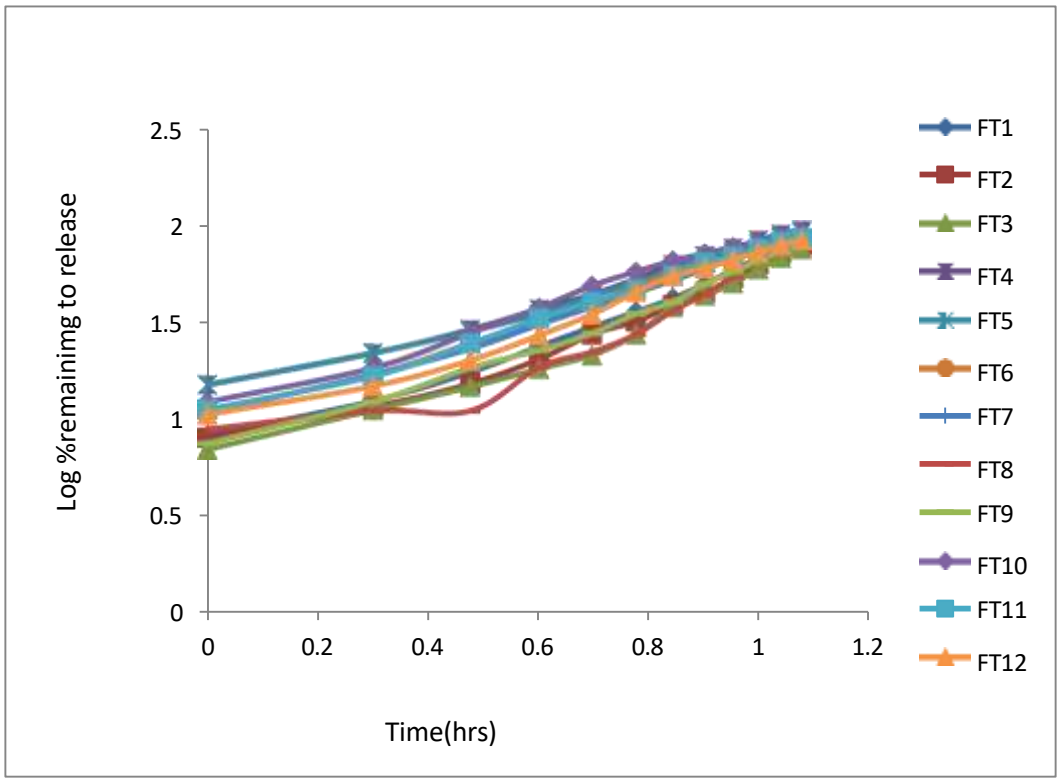


Fig: 13 Peppas release kinetics profile of Glipizide floating tablets of batches F1 to F12.

Different Drug Release Kinetics Model For Glipizide Floating Tablets

Table 16 Regression coefficients fit to different drug release kinetics models for Glipizide floating tablets.

Formulation code	Zero order	First order	Higuchi	Peppas	
	r^2	r^2	r^2	r^2	n
F1	0.917	0.942	0.910	0.974	0.904
F2	0.985	0.902	0.865	0.970	0.969
F3	0.977	0.990	0.848	0.963	0.993
F4	0.994	0.916	0.952	0.990	0.780
F5	0.992	0.930	0.951	0.989	0.767
F6	0.995	0.943	0.940	0.995	0.878
F7	0.997	0.916	0.930	0.994	0.867
F8	0.960	0.857	0.818	0.928	0.956
F9	0.992	0.922	0.885	0.986	0.979
F10	0.983	0.955	0.956	0.990	0.863
F11	0.996	0.958	0.942	0.994	0.865
F12	0.995	0.959	0.922	0.978	0.910

In-vitro buoyancy studies of the Glipizide floating tablet

At (92 sec) After 12 hrs

Fig 14 *In-vitro buoyancy* studies of the Glipizide floating tablet using HPMC K4M (F1)

At (41 sec) After 12 hrs

Fig 15 *In-vitro buoyancy* studies of the Glipizide floating tablet using Sodiumalginate (F4)

At (144 sec) After 12 hrs

Fig 16 *In-vitro buoyancy* studies of the Glipizide floating tablet using Sodiumalginate & Carbopol 940 (F7).

At (67 sec) After12 hrs

Fig 17 *In-vitro buoyancy* studies of the Glipizide floating tablet using HPMC K4M& Carbopol 940 (F10).

Discussion

In the present study, Gastroprotective drug delivery systems of Glipizide were prepared by using different viscosity grades of hydroxy propyl methyl cellulose (HPMC), viz., K4M and Sodium alginate, and Xanthan gum at different drug to polymer ratios with gas generating agent like sodium bicarbonate. The weighed quantities of drug and polymers were mixed thoroughly in different ratios and tablets were prepared by direct compression method. The prepared tablets were evaluated for its hardness, friability, uniformity of weight, uniformity of drug content, drug-polymer interaction studies, *in vitro* floating studies, *in-vitro* dissolution studies. The melting point of Glipizide was found to be 197-199°C, which complied with BP standards thus indicating purity of obtained drug sample. Based on preliminary identification test it was concluded that the Glipizide complied the preliminary identification. By scanning the drug in U.V spectrophotometer in 200-400 nm range, a sharp peak was observed at 220 nm using 0.1 N HCL as solvent. It was concluded that the drug has λmax 220 nm (as per I. P) as showed in fig .1. From the standard curve of Glipizide, it was observed that the drug obeys Beer's law in the range 2-20 µg/ml and the equation was generated it was showed fig 2 and table1. The drug-polymer interaction study was carried out using FTIR (KBr pellet method) FTIR drug-polymers interaction studies are shown in fig 3 to 6 and reported in table 2. It was found that Glipizide was compatible with HPMC K4M, Sodium alginate, and Xanthan gum, used in the formulation, there were no extra peaks observed. Thus, the chosen polymers for the formulations were found to be compatible with Glipizide and have no physical interaction. The angle of repose of the drug powder was in the range of 21.54 to 24.06, the Carr's index was found to be in the range of 11.42 to 17.67 indicating compressibility of the tablet. Haunser's ratio was found in the range of 1.12 to 1.20 is good as reported in table 4. Prepared tablets were evaluated for weight variation and percentage deviations from the average weight are reported in table 5 and was found to be within the prescribed official limits. The friability of the formulations as found to be between 0.59 to 0.78 is reported in table 5 and as that of which was found to be within the official requirement (i.e.,

not more than 1%). The thickness of the tablet indicates that die fill was uniform. The thickness depends upon the size of the punch and the weight of the tablet (200 mg). The thickness of the batch from F1-F12 was found to be 2.12-2.94 mm and hardness was found to be 4.3-5.0 Kg/cm2 as reported in table 5 which had good mechanical strength. The Percentage of drug content for F1 to F12 was found to 94.513±0.130 to 99.672±0.612 of Glipizide, it complies with official specifications. The results were shown in table 5. On immersion in 0.1 N HCL solution pH (1.2) at 37^0C, the tablets floated, and remained buoyant without disintegration. Fig 14 to 17 shows Buoyancy character of prepared tablet. From the results it can be concluded that the batch containing HPMC K4M polymer showed good floating lag time (FLT). Formulation containing HPMC K4M, Sodium alginate showed less FLT compared to formulation containing Xanthan gum. *In-vitro dissolution* studies were performed for all the batches of tablets containing Glipizide using USP XXIII dissolution test apparatus-II at 50 rpm, with 900 ml of 0.1N HCl used as dissolution media. The *in-vitro* drug release data is given in tables 6–16, and drug release profiles are shown in figs. 9–13. Formulations F1, F2, and F3 containing drug and HPMC K4M exhibited 82.356±0.182, 79.812±0.135, and 75.624±0.219 of drug release after 12 hours, respectively, and the data is given in Table 6 and drug release profiles are shown in Fig 9. Formulations F4, F5, and F6 containing the drug polymer sodium alginate exhibited 95.083±0.457, 91.542±0.782, and 88.812±0.314 of drug release in 12 hours, respectively, and the data is given in Table 6 and drug release profiles are shown in Fig 9. Formulations F7, F8, and F9 containing drugs and polymers like sodium alginate and xanthan gum exhibited 88.621±0.414, 82.356±0.306, and 79.521±0.423 of drug release in 12 hours, respectively, and the data is given in Table 5.7, and drug release profiles are shown in Fig. 9. Formulations F10, F11, and F12 containing drugs and polymers like HPMC K4M and Xanthan gum exhibited 92.354±0.864, 85.624±0.367, and 83.731±0.537 of drug release in 12 hours, respectively. The data is given in Table 7, and drug release profiles are shown in Fig. 9. The *in-vitro* drug release data was subjected to analysis according to zero order, first order kinetic equations, Higuchi and Peppas models to ascertain the mechanism of drug release. The results of linear regression analysis of data including regression coefficient are summarized in table 16. When the regression coefficient 'r' value of zero order and first order plots were compared, it was observed that the 'r' values of zero order were in the range of 0.917 to 0.997 whereas the 'r' values of first order plots were found to be in the range of 0.857 to 0.990 indicating drug release from all the formulations were found to follow zero order kinetics. The Higuchi's plot has shown with the regression values in the range of 0.818 to 0.952 shown in table no 12 and 13 The *in-vitro* dissolution data as log cum percent drug release versus log time were fitted to Peppas, values of the exponent 'n' was found to be in the range of 0.767 to 0.993 indicating that the drug release is by non-Fickian diffusion mechanism.

Conclusion

Compatibility studies have confirmed that HPMC K4M, Xanthan gum, and Sodium alginate are suitable excipients for formulating Glipizide floating tablets. These tablets were fabricated using the direct compression method. In-vitro buoyancy studies, conducted using 0.1 N HCl solution at 37°C, revealed that the tablet formulation containing HPMC (F4) exhibited excellent buoyancy, characterized by a very short lag time and prolonged floatation time exceeding 12 hours. In-vitro release studies, conducted over a 12-hour period, identified the optimized formula containing Sodium alginate (F4) as having superior release characteristics compared to other formulations, following zero-order kinetics. The drug release mechanism from this formulation was confirmed to be non-Fickian diffusion. This study concludes that Sodium alginate is an effective polymer for developing a Glipizide sustained-release gastro-retentive floating drug delivery system (FDDS). Additionally, the viscosity of the polymer was identified as a critical factor influencing both the drug release and floating properties of the FDDS.

Conflict of interest

None

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