Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 3, Suppl 4, 2011

Research Article

FORMULATION AND EVALUATION OF SINTERED GASTRO RETENTIVE TABLETS OF GLIPIZIDE

B. SESHAGIRI*[1], DR. K. A. CHOWDARY[2], Y. DEEPTHI PRIYA[3]

[1.] Aurobindo Pharma Limited, Hyderabad, A.P, [2.] St. Ann's College of Pharmacy, Contonment, Vizianagaram, A.P, [3.] Arya College of Pharmacy, Kandi, Sangareddy, Medak (D), A.P. Email: gorantla.giri@gmail.com

Received: 1 May 2011, Revised and Accepted: 12 June 2011

ABSTRACT

Hydrodynamically Balanced Systems (HBS) with sintering technique is an approach to increase the gastric residence time of drugs in stomach. This system is designed for site specific oral drugs with low bulk density than gastric fluids so as to buoyant the dosage form in stomach to increase the residence time of the drug. In the present investigation, an attempt was made to design hydrodynamically balanced drug delivery systems for Glipizide using HPMC K_4M and HPMC $K_{15}M$ polymers by solvent casting sintering technique. Various batches of matrix tablets of Glipizide were prepared with varying concentrations of polymers using direct compression method which were exposed to different time periods under saturated acetone vapour system for sintering.

The tablets so designed were evaluated for physical characteristics, drug content, floating time, floating lag time, etc. The study reveals that the formulations of HBS of Glipizide formulated has exhibited a floating lag time of less than 5 minutes and floating time of more than 22 hrs. From the In-Vitro drug release studies (USP XXIII), the matrix tablets containing HPMC $K_{15}M$, which was exposed to acetone vapors for a period of 4.5 hrs, showed 69.17% drug release in 12 hrs and showed better control of drug release in comparison with the marketed preparation. The in-vitro release data was treated with mathematical equations, and was concluded that Glipizide released from the tablet followed Peppas model with non-Fickian diffusion. The results indicate that gas powered Hydrodynamically Balanced Tablets of Glipizide containing HPMC $K_{15}M$ provides a better option for controlled release action and improved bioavailability.

Keywords: Gastric residence, Gas generation, Floating, Glipizide, HPMC, Release kinetics, Diffusion models.

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral controlled drug delivery systems provides the continuous delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either a local or systemic action.

Conventional oral controlled dosage forms suffer from mainly two adversities like short gastric retention time (GRT) and unpredictable gastric emptying time. A relatively brief GI transit time of most drug products (8 -12 h) impedes the formulation of single daily dosage forms. These problems can be overwhelmed by altering the gastric emptying. Therefore it is desirable to formulate a controlled release dosage form that gives an extended GI residence time. [1, 2]

A number of approaches have been used to increase the GRT of a dosage form in stomach by employing a variety of concepts. Various gastro retentive techniques were used including floating, swelling, high density and bioadhesive systems.[3]

Floating Drug Delivery Systems (FDDS) have a bulk density lower than gastric fluids and thus remain buoyant in the stomach for a prolonged period of time, without affecting the gastric emptying rate. While the system is floating on the gastric contents, the drug is released slowly at a desired rate from the system. This results in an increase in the GRT and a better control of fluctuations in the plasma drug concentrations.[4]

Sintering means fusion of particles or formulations of welded bonds between particles of polymer. Controlled release oral dosage forms were developed by sintering the polymer matrix either by exposing to temperature above the glass transition (Tg) point of the polymer or exposing these matrix systems to solvent vapours.[5, 6]. In the present investigation, an attempt was made to use the solvent casting method for sintering the tablets.

Glipizide is an oral anti-diabetic drug which belongs to sulfonylurea class having narrow range of effective blood concentration and short elimination half-life in humans and hence, it is suitable for a sustained release form. Since the drug Glipizide has site specific absorption in the upper part of the stomach, it was used as a model drug to prepare gastro retention tablets.[7]

Hence, in the present study it was aimed to test the suitability of using Hydroxypropyl Methylcellulose in the development of floating drug delivery systems and for controlling the drug release from the matrix tablets prepared by using sintering technique with the help of solvent.

MATERIALS AND METHODS

Materials

The following materials were used in the study: Glipizide BP (Micro Lab Ltd., Bangalore), HPMC K_4M (Sri Dev Pharmaceuticals, Hyderabad), HPMC $K_{15}M$ (Aurobindo Pharma Ltd., Hyderabad), Sodium bicarbonate, Lactose Monohydrate, Acetone (S.D. Fine Chem. Ltd) and Magnesium Stearate (Loba Chemie). All other chemicals used were of reagent grade.

Preparation of Matrix tablets of Glipizide

Floating matrix tablets containing Glipizide were prepared by direct compression technique using varying concentrations of different grades of polymers with sodium bicarbonate.

All the ingredients except magnesium stearate were blended in glass mortar uniformly. After sufficient mixing of drug as well as other components, magnesium stearate was added and further mixed for additional 2-3 minutes. The tablets were compressed with 13 mm circular punch using hydraulic press. Compression force of the machine was adjusted to obtain the hardness in the range of 3-4 kg/cm^2. The weight of the tablets was kept constant for formulations F_1 to F_{12}. The compositions of all formulations were given in Table 1.

After the preparation, sintering technique was carried for the prepared tablets. In this method, the tablets were exposed to acetone vapors at different time intervals kept in a dessicator filled with acetone at the bottom and equilibrated for 24 hrs for varying time periods. The reason for selecting acetone as the solvent is due to the partial solubility of HPMC in acetone as complete solubility would dissolve the polymer and insolubility would not serve the purpose of sintering.

Table 1: Composition of Hydrodynamically Balanced tablets of Glipizide

Ingredients*	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Glipizide	13	13	13	13	13	13	13	13	13	13	13	13
HPMC K_4M	200	200	200	200	---	---	---	---	100	100	100	100
HPMC $K_{15}M$	---	---	---	---	200	200	200	200	100	100	100	100
Sodium bicarbonate	20	20	20	20	20	20	20	20	20	20	20	20
Lactose	70	70	70	70	70	70	70	70	70	70	70	70
Magnesium stearate	7	7	7	7	7	7	7	7	7	7	7	7
Sintering Time (hrs)	--	1.5	3.0	4.5	--	1.5	3.0	4.5	--	1.5	3.0	4.5

*All the ingredients are in milligrams per tablet

Buoyancy / Floating Test

The buoyancy of the tablets was studied at 37±0.5° C, in simulated gastric fluid at pH 1.2. The time between introduction of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT). The buoyancy of the tablets was studied in 0.1N HCl at 37±0.5°C.

Swelling Study[8]

The swelling behavior of a dosage form was measured by studying its weight gain or water uptake. The dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake was measured in terms of percent weight gain, as given by the equation.

$$W = \frac{(Wt - Wo)}{Wo} \times 100$$

Wt = Weight of dosage form at time t

Wo = Initial weight of dosage form

Test for Content Uniformity

Glipizide tablets containing 13 mg of drug was dissolved in 100 mL of 0.1N HCl and kept for sonication. The solution was filtered, 1mL of filtrate was taken in 50 mL of volumetric flask and diluted up to mark with 0.1N HCl and analyzed spectrophotometrically at 233 nm. The concentration of Glipizide in mg/ml was obtained by using standard calibration curve of the drug. Claimed drug content was 13 mg per tablet. Drug content studies were carried out in triplicate for each formulation batch.

Effect of hardness on Buoyancy Lag Time (BLT) or Floating Lag Time[9]

Formulation F_5 was selected to study the effect of hardness on buoyancy lag time. The tablets of batch F_5 were compressed at four different compression pressures to get the hardness of 4 kg/cm^2, 5 kg/cm^2, 6 kg/cm^2 and 7 kg/cm^2. The tablets were evaluated for Buoyancy Lag Time. The method followed is same as that of Buoyancy test.

In-vitro Dissolution Study

In-vitro release studies were carried out using USP XXIII dissolution test apparatus. 900 mL of 0.1N HCl (pH 1.2) was filled in dissolution vessel and the temperature of the medium was set at 37°±0.1°C. For the study ring/mesh assembly was used. The reason was that, when paddle apparatus was used, the tablets would rise and eventually stick to the flange of the rotating shaft resulting in partial surface occlusion. In case of basket apparatus, it was observed that after 5 - 7 hr the tablets had swollen to such an extent that they were completely constricted by the radius of the basket and completely filled the bottom of the basket. Once the dosage form completely fills the basket, tablet was unable to swell further and move in unimpeded fashion leading to limited drug release. In order to overcome these drawbacks ring mesh device was employed in the study. [10]

The tablet was kept inside the ring assembly and placed inside the dissolution vessel. The speed was set at 100 rpm. 5 mL of sample was withdrawn at predetermined time intervals for 12 hours and same volume of fresh medium was replaced. The samples were analyzed for drug content against 0.1N HCl as a blank at λmax 233 nm using UV spectrophotometer.

Data Analysis (Curve fitting analysis)[11]

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as:

1) Cumulative percentage drug released Vs time (In-Vitro drug release plots)

2) Cumulative percentage drug released Vs Square root of time (Higuchi's plots)

3) Log cumulative percentage drug remaining Vs Time (First order plots)

4) Log percentage drug released Vs log time (Peppas plots)

Scanning Electron Micro graphs of the optimized formulation

Morphological details on the specimens were determined by using SEM models GSM 35 CF Joel Japan. Conventional SEM sample preparation methods were applied for these studies. The samples were dried thoroughly in vacuum dessicator before mounting on a brass specimen studs. The samples were mounted using double sided adhesive tape and gold palladium alloy of 120 A0 thickness was coated on the sample using sputter coating unit in argon ambient of 8-10 with plasma voltage about 2KV and discharge current about 20 MA. The SEM was operated at low accelerating voltage of about 15 KV with a load current of about 80 MA. The condenser lens position was maintained at a constant level. Working distance was 39 mm; the photomicrographs were recorded at 500X, 1000X, 3000X and 4000X.

Comparison with marketed product

The promising formulation was compared with marketed Glipizide CR formulation.

RESULTS

Hydrodynamically balanced tablets of Glipizide were prepared and evaluated for their use as gastro retentive drug delivery systems to increase its local action and bioavailability. In the present work, total twelve formulations were prepared and complete compositions of all batches were shown in Table 3. The formulated tablets were then characterized for various physico-chemical parameters.

Pre-compression Parameters

Angle of Repose (θ)

The values obtained for angle of repose for F_1, F_5 and F_9 formulations are tabulated in Table 2. The values were found to be 24°.30', 26°.77' and 25°.28'. This indicates good flow property of the powder blend.

Compressibility Index

Compressibility index values for F_1, F_5 and F_9 formulations were 12.30, 15.67 and 15.41% respectively indicating that the powder blends have the required flow property for direct compression.

Post-compression Parameters

Tablet dimensions

The dimensions determined for formulated tablets were tabulated in Table 2. Tablets mean thicknesses were almost uniform in all the formulations and were found to be in the range of 5.14 mm to 5.18 mm. The diameter of the tablet ranges between 11.02 mm to 11.21 mm.

Weight Variation Test

The percentage of weight variations for all formulations was shown in Table 2.

All the tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits. The weights of all the tablets were found to be uniform with low standard deviation values.

Table 2: Physical properties of tablets of batches F_1, F_5 and F_9

Batch No.	Angle of Repose (θ)	Compressibility Index (%)	Diameter (mm)	Thickness (mm)	Wt. variation (mg)	Drug Content Uniformity (%)
F_1	24°.30'	12.30	11.19 ± 0.04	5.16 ± 0.08	312 ± 1.29	98.71
F_5	26°.77'	15.67	11.20 ± 0.06	5.14 ± 0.02	307 ± 1.34	97.12
F_9	25°.28'	15.41	11.22 ± 0.05	5.18 ± 0.02	311 ± 1.49	99.50

Hardness test

The measured hardness of tablets for each batch ranges from 3.6 kg/cm^2 to 4.3 kg/cm^2 (Table 3). Tablet hardness was increased with increase in the sintering time. This ensures good handling characteristics of all batches.

Friability Test

The values of friability test were tabulated in Table 3. Tablets exposed to acetone vapors for a greater period showed the least friability as compared to the tablets that were unsintered. Therefore, by using this technique of sintering the friability of tablets can be reduced to a greater extent. The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

Table 3: Hardness and Friability

Parameter	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Hardness (kg/cm^2)	3.6 ± 0.21	3.6 ± 0.20	3.7 ± 0.30	3.9 ± 0.06	3.9 ± 0.05	4.0 ± 0.07	4.1 ± 0.50	4.3 ± 0.42	3.8 ± 0.50	3.8 ± 0.04	3.9 ± 0.54	4.0 ± 0.12
Friability (%)	0.63	0.41	0.38	0.20	0.28	0.24	0.18	0.04	0.48	0.38	0.31	0.12

Tablet density

To provide good floating behavior in the stomach, the density of the device should be less than that of the gastric contents (1.004 g/cm^3). All the batches showed density below than that of gastric fluid (1.004). The values are shown in Table 4. When the tablet contacts test medium, tablet gets expanded (because of swellable polymers) and there was liberation of CO_2 gas (because of effervescent agent, $NaHCO_3$). The density decreased due to this expansion and upward force of CO_2 gas generation. This plays an important role in ensuring the floating capability of the dosage form.

Table 4: Tablet Density, Buoyancy Lag Time and Total Floating Time

Batch No.	Tablet Density (g/cc)	Buoyancy Lag Time (minutes)	Total Floating Time (hrs)
F_1	0.96	5 min 21 sec	> 20
F_2	0.94	5 min 11 sec	> 20
F_3	0.93	4 min 48 sec	> 20
F_4	0.89	4 min 05 sec	> 20
F_5	0.90	4 min 22 sec	> 24
F_6	0.88	4 min 12 sec	> 24
F_7	0.85	3 min 45 sec	> 24
F_8	0.82	3 min 14 sec	> 24
F_9	0.95	4 min 40 sec	> 22
F_{10}	0.92	4 min 26 sec	> 22
F_{11}	0.88	4 min 13 sec	> 22
F_{12}	0.87	4 min 07 sec	> 22

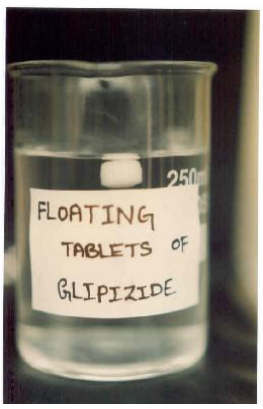

Fig. 1: Picture depicting the floating tablet of Glipizide

Buoyancy Study

On immersion in solution of 0.1N HCl with pH 1.2 at 37° C, the tablets floated and remained buoyant without disintegration. Table 4 shows the results of Buoyancy study and Fig. 1 show Buoyancy character of prepared tablet. From the results it can be concluded that the batch containing only HPMC $K_{15}M$ polymers showed good Buoyancy lag time (BLT) and Total floating time (TFT). Buoyancy lag times of the formulations were found to decrease as the time of sintering was increased. Formulation F_8 containing HPMC $K_{15}M$ and exposed to acetone vapors for 4.5 hrs showed good BLT of 3 min 14 sec and TFT greater than 24 hrs.

in Fig. 2. Buoyancy of the tablet was governed by both the swelling of the hydrocolloid particle on surface when it contacts the gastric fluid which in turn results in an increase in the bulk volume and the presence of internal void space in the dry center of the tablet (porosity). Increase in the hardness of the tablets, results in increased buoyancy lag time which might be due to high compression resulting in reduction of porosity of the tablet and moreover, the compacted hydrocolloid particles on the surface of the tablet cannot hydrate rapidly when the tablet reaches the gastric fluid and as a result of this, the capability of the tablet to float is significantly reduced.

Swelling Study

Swelling ratio describes the amount of water that is contained within the hydrogel at equilibrium and is a function of the network structure, hydrophilicity and ionization of the functional groups. Swelling study was performed on F_1, F_5, F_9 batches for 5 hr. The results of swelling index are given in Table 5.

From the results it was concluded that swelling increases as the time passes because the polymer gradually absorb water due to hydrophilicity of polymer. The outermost hydrophilic polymer present in the tablet matrix hydrates swells and forms a gel barrier. As the gelatinous layer progressively dissolves and/or is dispersed, the hydration swelling release process is repeated towards new exposed surfaces, thus maintaining the integrity of the dosage form.

In the present study, the higher swelling index was found for tablets of batch F_5 containing HPMC $K_{15}M$ having nominal viscosity of 15,000 cps. Thus, the viscosity of the polymer had major influence on swelling process, matrix integrity as well as floating capability. Hence from the results it can be concluded that linear relationship exists between swelling process and viscosity of polymer.

Table 5: Swelling Index of Tablets of Batch F_1, F_5 and F_9

Time (hrs)	Swelling Index (%)		
	F_1	F_5	F_9
1	80	82	79
2	129	135	130
3	148	162	156
4	168	185	172
5	185	207	189

Drug Content Uniformity

The percentage of Glipizide content in the prepared tablets was found to be 97.12% to 99.5%, which was within the acceptable limits. Table 2 showed the results of drug content uniformity in each batch.

Effect of hardness on Buoyancy Lag Time

The effect of hardness on buoyancy lag time for batch F_5 was studied because it showed buoyancy lag time of 59 sec at hardness of 4 kg/cm^2.

The results of floating lag time of tablet having hardness of 4 kg/cm^2, 5 kg/cm^2, 6 kg/cm^2 and 7 kg/cm^2 were 4 min 22 sec, 5 min 37 sec, 7 min 11 sec and 10 min 45 sec respectively as tabulated in Table 6. The plot of floating lag time (sec) V/s hardness (kg/cm^2) is depicted

Table 6: Effect of Hardness on Buoyancy Lag Time of Batch F_5

Hardness (kg/cm^2)	Buoyancy Lag Time (sec)
4 kg/cm^2	262 sec
5 kg/cm^2	337 sec
6 kg/cm^2	431 sec
7 kg/cm^2	645 sec

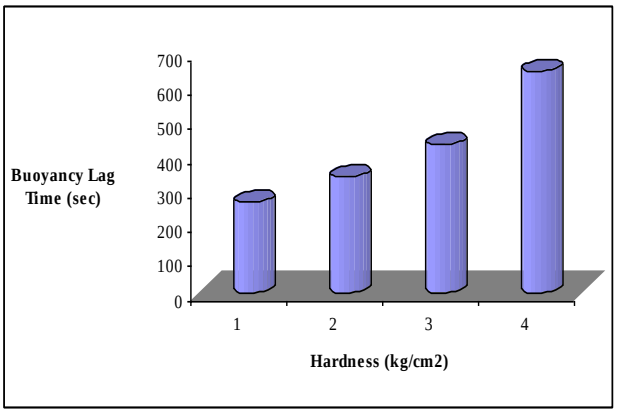

Fig. 2: Effect of hardness on Buoyancy Lag Time

In-vitro Dissolution Study

The in-vitro drug release profiles of tablet from each batch (F_1 to F_{12}) were carried in 0.1N HCL having pH 1.2 for 12 hrs by using ring mesh device. Percentage drug release from all the formulations were shown in the Table 7 and the plot of % Cumulative drug release Vs time (hr) was plotted and depicted as shown in Fig. 3, 4 and 5.

Table 7: In-Vitro drug release profile of Glipizide from all formulations

Batch No.	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Time (hrs)	% Drug Released											
0.3	27	24	19	17	22	17	12	7	24	20	17	12
1	34	28	23	22	30	19	19	10	31	25	23	20
2	37	35	34	30	38	27	25	15	34	31	27	24
3	53	41	38	32	51	34	30	28	50	48	44	38
4	56	55	45	43	57	38	37	38	53	51	48	44
5	61	58	53	48	61	59	38	44	59	57	54	48
6	70	64	58	56	68	61	53	48	67	64	63	51
7	74	70	64	61	77	74	57	52	70	69	64	57
8	79	75	73	70	83	79	64	57	76	71	72	60
9	83	80	77	82	86	83	70	59	80	79	77	72
10	90	85	86	83	89	84	76	60	87	85	83	77
11	98	93	91	85	91	87	77	66	91	89	86	79
12	99	96	93	86	93	89	78	69	95	90	87	82

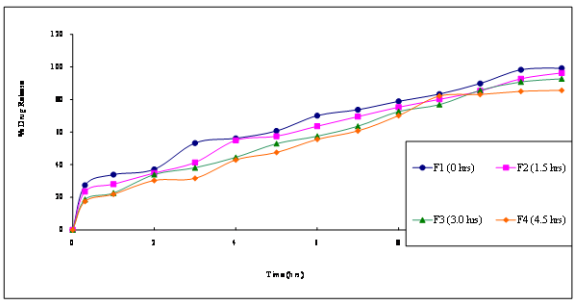

Fig. 3: In-Vitro drug release of Glipizide for F_1, F_2, F_3 and F_4 formulations exposed to acetone vapors at different time intervals

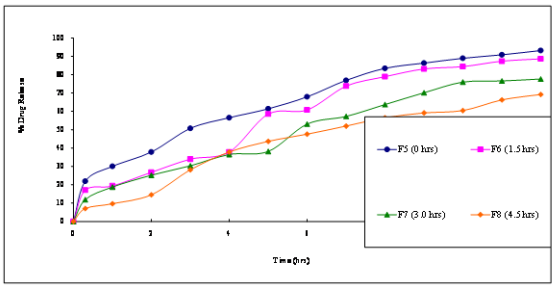

Fig. 4: In-Vitro drug release of Glipizide for F_5, F_6, F_7 and F_8 formulations exposed to acetone vapors at different time intervals

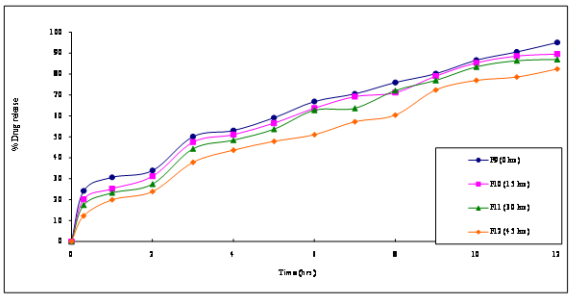

Fig. 5: In-Vitro drug release of Glipizide for F_9, F_{10}, F_{11} and F_{12} formulations exposed to acetone vapors at different time intervals

From the in-vitro dissolution data, it was found that the drug release studies from formulations containing HPMC $K_{15}M$ sintered for 1.5, 3.0 and 4.5 hrs, the cumulative percentage releases were 88.58, 77.58 and 69.17% respectively and 93.11% for unsintered tablet. Formulations containing HPMC K_4M, sintered for 1.5, 3.0 and 4.5 hrs, the cumulative percentage release was 96.34, 92.78 and 85.67% respectively and 99.25% for unsintered tablets. While the formulations containing both polymers sintered for 1.5, 3.0 and 4.5 hrs, the cumulative percentage release was 89.55, 86.96 and 82.43% respectively and 95.05% for unsintered tablets.

Curve Fitting Analysis

The results of dissolution data was fitted to various drug release kinetic equations. Peppas model was found to be the best fitted in all dissolution profiles having higher correlation coefficient (r-value) followed by Higuchi model and First order release equation. The kinetic values obtained for different formulations are tabulated in Table 7. Korsemeyer-Peppas model indicates that release mechanism is not well known or more than one type of release phenomena could be involved. 'n' value could be used to characterize different release mechanisms and in the present study 'n' value ranges from 0.5 to 1 for all the batches. So, it was concluded that the drug release occurred via non-Fickian diffusion, which shows that the release from initially dry, hydrophilic glassy polymers that swell when added to water and become rubbery show anomalous diffusion as a result of the rearrangement of macromolecular chains.

Table 6: Curve fitting data for all formulations

Batch No.	First order Equation			Higuchi's Equation			Peppas Equation	
	Slope	Rate constant (K) mg. hr^{-1}	Regression coefficient (r)	Slope	Rate constant (K) mg. hr^{-1}	Regression coefficient (r)	Slope	Regression coefficient (r)
F_1	-0.1317	-0.303	0.8104	25.958	25.958	0.9780	0.5785	0.9817
F_2	-0.0978	-0.225	0.8905	26.341	26.341	0.9784	0.5687	0.9919
F_3	-0.0868	-0.199	0.9264	27.229	27.229	0.9715	0.607	0.9831
F_4	-0.0725	-0.166	0.9518	26.735	26.735	0.9553	0.6686	0.9697
F_5	-0.0914	-0.210	0.9868	26.453	26.453	0.9894	0.5631	0.9858
F_6	-0.0821	-0.189	0.976	29.158	29.158	0.9523	0.7313	0.9599
F_7	-0.0555	-0.127	0.9748	25.089	25.089	0.9642	0.6975	0.9742
F_8	-0.0415	-0.0955	0.988	23.275	23.275	0.9792	0.7762	0.9812
F_9	-0.0897	-0.206	0.9305	25.389	25.389	0.9841	0.5845	0.9839
F_{10}	-0.077	-0.177	0.972	25.854	25.854	0.9855	0.6482	0.9884
F_{11}	-0.0717	-0.165	0.9791	26.184	26.184	0.9831	0.6082	0.9823
F_{12}	-0.0588	-0.135	0.972	25.11	25.11	0.9794	0.6486	0.9867

Stability Studies

The selected formulation (F_8) was tested for 8 weeks at the storage conditions of 25^0 C and 40^0 C at 60 % RH and 75 % RH respectively, were analyzed for their drug content. The residual drug contents of formulations were found to be within the permissible limits as shown in the Table 7.

The tablets were also subjected to IR studies to determine compatibility of the drug with the excipients used in the tablets. The IR studies showed that there are no interactions between the drug and polymers.

Scanning electron microscope

Fig. 6 depicts the cross section and pore formation of the gelled matrix of a tablet after swelling in the dissolution medium. Hence, it proves integrity of the membrane after swelling and this ensures the flow of drug through the gelled matrix tablet is by diffusion mechanism.

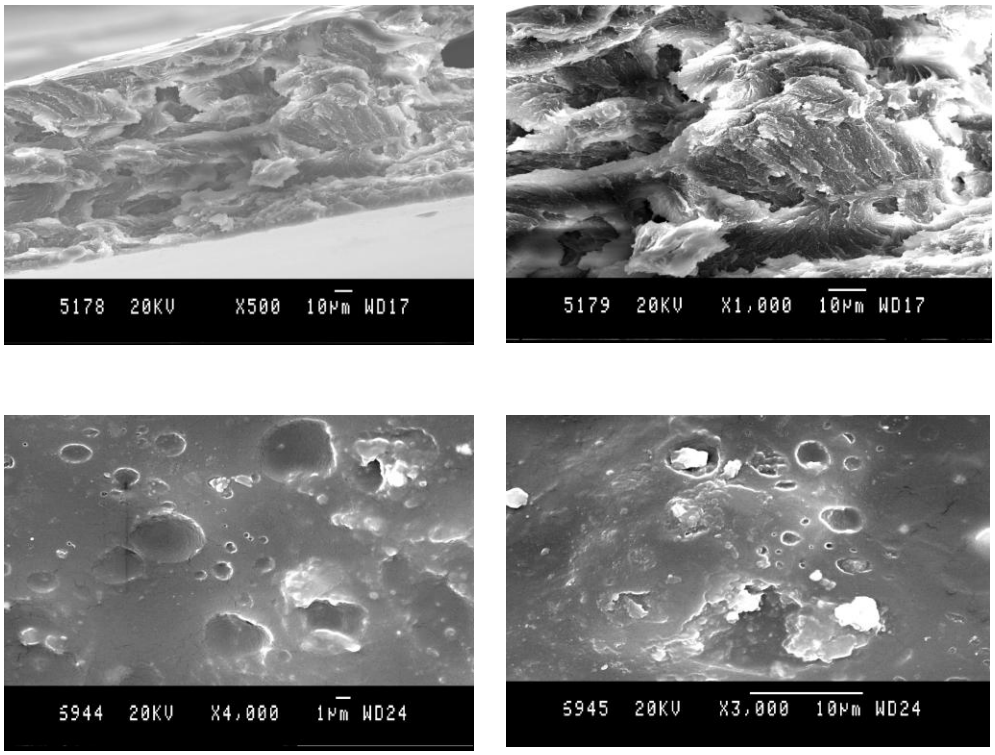

Fig. 6: Photographs Showing the Scanning Electron Microscopy of Gelled Matrix

Table 7: Stability data of F_8 formulation

Time in weeks	Formulation F_8			
	Stored at 25°C/ 60% RH		Stored at 40°C/ 75% RH	
	Physical Appearance	% Drug Content	Physical Appearance	% Drug Content
0	+++	97.58	+++	97.61
2	+++	96.98	+++	94.47
4	+++	97.95	+++	96.81
6	+++	96.98	++	95.89
8	++	95.75	++	94.21

+++ = Same as on zero day, ++ = Slight change in colour

Comparison with Marketed Product

The promising formulation (F_8) as found by evaluation studies was compared with marketed product Glipizide CR. The marketed product gave 92.78% of drug release in 12 hrs of dissolution study.

In-vitro dissolution profile of marketed product in comparison to the formulation F_8 were shown graphically in Fig. 7 and showed that the formulation F_8 with 69.17% of drug release has better control over release of drug in comparison with marketed product.

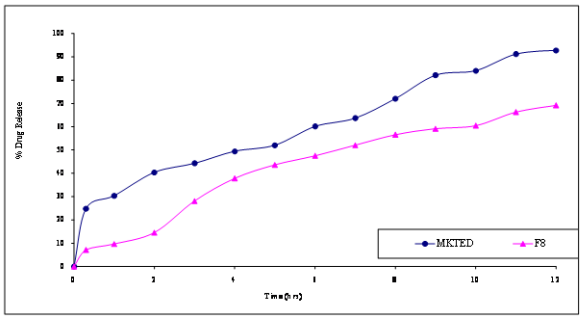

Fig. 7: Comparative drug release profiles between marketed product and F_8 formulation

DISCUSSION

In the present investigation gastric retentive system of Glipizide were prepared with HPMC K_4M and HPMC $K_{15}M$ polymers. Glipizide has site-specific absorption in the upper part of the stomach and hence these systems are useful in the improving the absorption of the drug. Release of the drug from the tablets prepared with HPMC K_4M and HPMC $K_{15}M$ polymers was controlled by sintering with acetone solvent method, which avoids the thermal degradation of the drug. Hydrodynamically Balanced Tablets of Glipizide could be formulated as an approach to increase gastric residence time and thereby improve its bioavailability. HPMC K_4M and HPMC $K_{15}M$ matrix tablets of Glipizide were prepared by direct compression technique and the tablets were exposed to acetone vapors in a desiccator filled with acetone at the bottom for the time intervals for a period of 1.0, 3.5 and 4.5 hrs. Formulated tablets gave satisfactory results for various physicochemical parameters like Tablet dimensions, Hardness, Friability, Weight variation, Tablet density, Swelling index and Content uniformity. FT-IR studies revealed that there are no chemical interactions between Glipizide and the polymers used in the study. Among all the batches, tablets of batch F_8 possessed quick buoyancy lag time and good total floating time. Variation on hardness on tablet of batch F_5 was found to effect the floating lag time of the tablet as hardness increased. The dissolution profiles for Glipizide made with HPMC K_4M and HPMC $K_{15}M$, showed that the use of these polymers permit efficient control of the release of the drug. The observed formulation difference in dissolution rates can be attributed to differences in the viscosity-enhancing effect of the HPMC and also the drug: HPMC ratio. The tablets made with lower polymer content and lower viscosity have faster dissolution rates, thus increasing the dissolution of drug. The effect of sintering time on the drug release from matrix tablets was evaluated and it was found that the time of sintering is proportional to the amount of drug release. From all the formulations, F_8 containing HPMC $K_{15}M$, which is exposed to acetone, vapors for about 4.5 hrs showed extended drug release. The kinetics of drug release and the release mechanism from sintered matrix tablets were ascertained and found to be First-order and the mechanism of drug release followed Peppa's diffusion model. Formulation F_8 has better controlled drug release in comparison to marketed product.

CONCLUSION

In the present study Gastro retentive delivery systems of Glipizide were successfully developed in the form of Hydrodynamically Balanced Tablets to improve the local action and ultimately its bioavailability.

REFERNCES

1. Robinson JR, Lee V.H.L., "Controlled drug delivery: fundamentals and applications", 2nd edition, New York: Marcel Dekker; 1978.
2. Caldwell LJ, Gardner RC, Cargill RC., "Drug delivery device which can be retained in the stomach for a controlled period of time". US Patent No. 4,767, 627; Aug 30, 1988.
3. Anilkumar J. Shinde, Arun N. Waghule, Manoj B. Paithane, Harinath N. More, "Formulation and In Vitro Evaluation of Sustained Release Floating Tablet of Cephalexin Using

Hydrophilic Polymers", International Journal of Pharmacy and Pharmaceutical Sciences, Vol 2, Suppl 2, 2010, 58-65.

4. Rosa M, Zia H, Rhodes T. Design and testing in vitro of a bioadhesive and floating drug delivery system for oral application. Int. J Pharm. 1994; 105:65-70.
5. B Sreenivasa Rao, A Seshasayana, K Himasankar, Y Prasanna Raju, K.V Ramana Murthy, "Design and Evaluation of Ethylene Vinyl Acetate Sintered Matrix Tablets", Ind. J. Pharm. Sci., Sept-Oct 2003, 496-502.
6. B Sreenivasa Rao, Y Prasanna Raju, L Srinivas, A Seshasayana, K Hima Sankar, B. Sirisha, K. V Ramana Murthy, "Design and Evaluation of Eudragit RL 100 Sintered Matrix Tablets", Indian J. Pharm. Sci., Mar-Apr 2004, 202-207.
7. Hardman JG, limbird L.E. Godman and Gilman's "The Pharmacological Basis of Therapeutics", 10th ed. New York; Mc Graw Hill; 2001.
8. El-Kamel AH, Sokas MS, Algamal SS., "Preparation and evaluation of Ketoprofen floating oral delivery system". Int. J. Pharm., 2001; 220: 13-21.
9. Praveen Nasa, Sheefali Mahant, Deepika sharma, "Floating systems: a novel approach towards Gastroretentive drug delivery Systems", International Journal of Pharmacy and Pharmaceutical Sciences, Vol 2, Suppl 3, 2010, 1-7.
10. Burns SJ, Altowood D, Barnwell SG., "Assesment of a dissolution vessel designed for use with floating and erodiable dosage forms", Int. J. Pharm 1998; 160: 213-18.
11. Ritger P. L., and Peppas, N. A., "The simple equation for description of solute release II. Fickian and anamalous release from swellable devices", J. Controlled Release, 1987, 5: 37-42.