www.ijrps.pharmascope.org

ISSN: 0975-7538
Research Article

Formulation and evaluation of gastroretentive floating bioadhesive tablets of glipizide

Rajesh Kumar Ranga*, P. Siva, Sajeeth C.I, Abdul Bari Mohd, K. Santhi

Department of Pharmaceutics, Grace College of pharmacy, Kodunthirapully, University of Calicut, Kerala, India

ABSTRACT

The purpose of present investigation was to develop and characterize a Novel Gastroretentive Drug Delivery System of Glipizide in the form of Floating and Bioadhesive Tablet which possesses a unique combination of floatation and bioadhesion properties. It was aimed to prepare for prolonged residence in the stomach over conventional Gastroretentive approaches. The tablets are produced by direct compression method by using HPMC K4M, HPMC K15M and HPMC K100M as hydrophilic polymers and Carbopol 974P as Bioadhesive polymer along with other requisite excipients in different combinations and proportions. Glipizide is a second-generation sulfonylurea drug which is typically prescribed to treat type II diabetes (non-insulin dependent diabetes mellitus). Its short biological half-life (3.4 ± 0.7 hours) necessitates that it be administered in 2 or 3 doses of 2.5 to 10 mg per day. Moreover, the site of absorption of Glipizide is in the stomach. Thus, the development of Gastroretentive dosage forms would clearly be advantageous. The prepared tablets were evaluated for different parameters such as thickness, hardness, weight uniformity, content uniformity, floating lag time, floating duration, swelling index, *in vitro* drug release, *ex vivo* bioadhesive strength, stability studies, and DSC, FTIR studies. The prepared tablets exhibited satisfactory physical parameters and good *in vitro* buoyancy. The modified *in vitro* assembly was used to measure the bioadhesive strength of tablets with fresh gastric mucosa of a goat as model tissue. Bioadhesion strength was increased with increase in the concentration of Carbopol. The tablets were evaluated for *in vitro* release in 1.2 pH buffer 0.1 N HCl. The *in-vitro* drug release of floating tablets (n=3) followed Fickian diffusion controlled release and are best explained by Higuchi equation. Carbopol 974P and HPMC K15M combination could be used to design effective and stable floating and bioadhesive tablets of Glipizide. The present study concludes that floating and bioadhesive tablets of Glipizide are potential dosage form due to its prolonged residence in stomach as compared to conventional stomach specific dosage forms.

Keywords: Glipizide; HPMC K4M; HPMC K15M; HPMC K100M; Carbopol 974P; Gastroretentive Floating Bioadhesive tablets.

INTRODUTION

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation. Many of the drug delivery systems, available in the market are oral drug delivery type systems. Oral drug delivery systems have progressed from immediate release to site-specific delivery over a period of time. Every patient would always like to have an ideal drug delivery system possessing the two main properties that are single dose or less frequent dosing for the whole duration of treatment and the dosage form must release active drug directly at the site of action. Thus the objective of the pharmacist is to develop systems that can be as ideal system as possible (Alexander Streubel, 2006).

Among all the methods described above for gastro retention, Floating drug delivery and bioadhesive drug delivery systems are taking the major part. But these two drug delivery systems are having two serious limitations, which has a great impact on the drug delivery to its intended site of administration.

Major disadvantage of floating system is requirement of a sufficient high level of fluids in the stomach for the drug delivery to float. The floating drug delivery systems are effective only when the fluid level in the stomach is sufficiently high. However, as the stomach empties and the tablet is at the pylorus, the buoyancy of the dosage form may be impeded.

And bioadhesive drug delivery systems are suffering from the effect of mucous turnover. The mucous secreted by the mucosa lining of stomach wall may detach the drug from the wall of stomach. Then the detached tablet may get emptied from the stomach along with its contents.

* Corresponding Author
Email: rangarajesh.1777@rediffmail.com
Contact: +91-9072898299, 9908582149
Received on: 25-02-2011
Revised on: 12-03-2011
Accepted on: 16-03-2011

Table 1: Composition of Glipizide Floating and Bioadhesive tablets

Formula code	Glipizide	HPMC K4M	HPMC K15M	HPMC K100M	Carbopol 974P	$NaHCO_3$	MCC	Mg Stea-rate	Talc
FM 1	10	70	-	-	30	35	52	2	1
FM 2	10	60	-	-	40	35	52	2	1
FM 3	10	50	-	-	50	35	52	2	1
FM 4	10	40	-	-	60	35	52	2	1
FM 5	10	30	-	-	70	35	52	2	1
FM 6	10	-	70	-	30	35	52	2	1
FM 7	10	-	60	-	40	35	52	2	1
FM 8	10	-	50	-	50	35	52	2	1
FM 9	10	-	40	-	60	35	52	2	1
FM 10	10	-	30	-	70	35	52	2	1
FM 11	10	-	-	70	30	35	52	2	1
FM 12	10	-	-	60	40	35	52	2	1
FM 13	10	-	-	50	50	35	52	2	1
FM 14	10	-	-	40	60	35	52	2	1
FM 15	10	-	-	30	70	35	52	2	1
F 1	10	100	-	-	-	35	52	2	1
F2	10	-	100	-	-	35	52	2	1
F3	10	-	-	100	-	35	52	2	1

Mg- Magnesium**, $NaHCO_3$-** Sodium bicarbonate**, MCC-** microcrystalline cellulose**, HPMC-** Hydroxypropyl methyl cellulose, all the ingredients are in mg per tablet and total weight of each tablet 200mg.

This serious limitation can be overcome by making the floating system eventually adhere to the mucous lining of stomach wall. Thus Floating and bioadhesive Drug Delivery System (FBDDS), thus, offers the advantage of increased gastric residence time of drugs over normal floating DDS. The FBDDS can be formulated by incorporating bioadhesive polymers to normal floating drug delivery systems (Cheueh H R, 1995).

Moreover, the site of absorption of Glipizide is in the stomach. Dosage forms that are retained in the stomach would increase the absorption, improve drug efficiency, and decrease dose requirements.

Due to its high permeability in nature controlled drug delivery is required for prolonged gastric retention may offer numerous advantages, including, increase in the extent of absorption, improved bio-availability and therapeutic efficacy.

MATERIALS AND METHOD

Materials

Glipizide, HPMC K4M, HPMC K15M and HPMC K100M, Sodium bicarbonate gift from Bright labs., Hyderabad; Carbopol 974p, Microcrystalline cellulose gift from Dr. Reddy's laboratories, Hyderabad; Talc, Magnesium Stearate S.D. Fine Chemicals, Mumbai.

Method

Preparation of Floating and Bioadhesive Tablets Glipizide

The Compositions of different formulation trials with different polymers are given in the following table 1. Accurately weighed quantities of hydrophilic polymers, Bioadhesive polymer, Microcrystalline Cellulose were taken in a mortar and mixed geometrically. To this mixture required quantity of Glipizide was added and mixed slightly with pestle. This mixture was passed through 40# and later collected in a plastic bag and blended for 5 min. To this required amount of sodium bi carbonate was added and again mixed for 5 min. Later sufficient quantity of Magnesium Stearate and Talc were added and the final blend was again passed through 40#. Thus obtained blend was mixed thoroughly for 10 min and compressed into tablets with 8.5 concave Punches and corresponding dies at a hardness of 6 kg/ cm single station tablet punching machine.

Preformulation Studies

Drug Excipients Compatibility Studies

The Successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients that are added to the formulation. The drug and excipients must be compatible with one another to produce a product that is stable, efficacious and safe.

IR spectroscopy

The physical properties of the physical mixture were compared with those of plain drug. Sample was mixed thoroughly with 100 mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 Psi for 3 minutes. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 4000 cm^{-1} to 625 cm^{-1} in a scan time of 12 minutes. The resultant spectra were compared for any spectral changes.

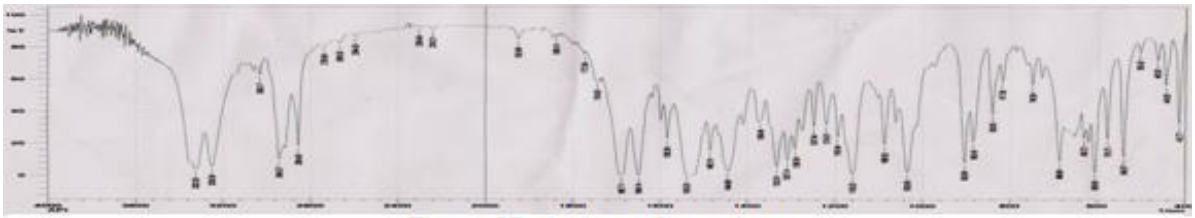

Figure: IR spectrum of pure drug

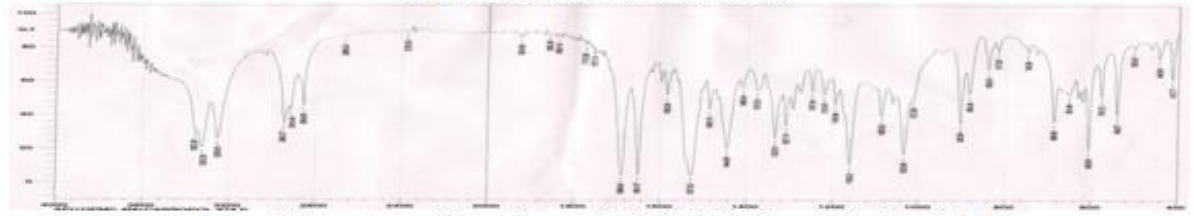

Figure: IR spectrum of pure drug with HPMC K4M and Carbopol 974P

Figure: IR spectrum of pure drug with HPMC K15M and Carbopol974P

Figure: IR spectrum of pure drug with HPMC K100M and Carbopol 974P

Figure 1: Drug Excipients Compatibility Studies by IR spectroscopy

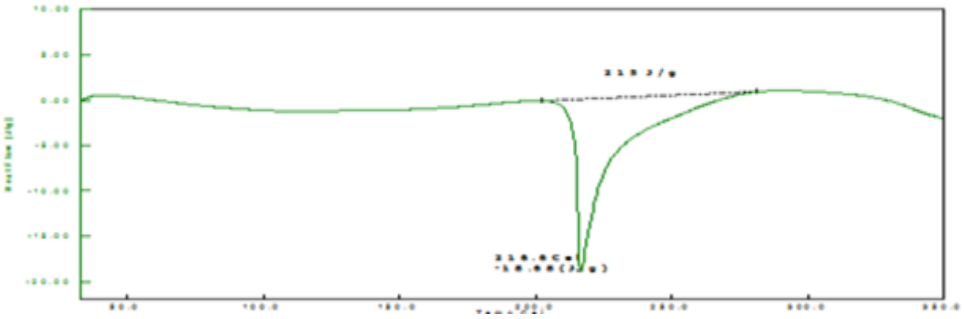

Figure 2: DSC of pure drug

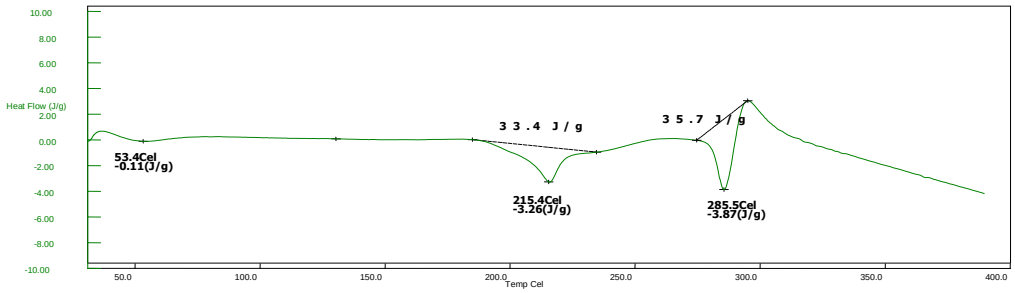

Figure 3: DSC of formulation FM8

The figure*:* 1 shows the results of IR spectrum of all the formulations of different excipients were shown no spectral changes when compared with pure drug hence it was excepted that there is no interaction with drug and with its formulations.

Differential scanning calorimetry (DSC)

DSC scan of samples were obtained in a Perkin Elmer thermal analyzer equipped with a monitor and printer. The instrument was calibrated with indium standard. Accurately weighed 5 mg of sample were placed in an open, flat bottom, Aluminum sample pans. Thermograms were obtained by heating the sample at a constant rate of 10°C/minute. A dry purge of nitrogen gas (20 ml/min) was used for all runs Samples heated from 35°C – 400°C.

Figure*:* 2 & 3 shows the results of formulation of FM 8, Thermographs obtained by DSC studies, revealed that the melting point of pure drug is 215.6°C and that Formulation of IRMTS shows sharp endothermic peak at 215.4°C as there is no much difference in melting point of the drug in the thermographs of the drug and that of in the formulation. It may be concluded that, the drug is in the formulation without interacting with the polymer and excipients.

Evaluation of Gastroretentive Floating Bioadhesive tablets of Glipizide

Evaluation of pre-compression parameters

The flow properties of pure drug were carried out and the results indicate that Glipizide [API] shows good flow, so it was decided to done by direct compression technique. Blend characterization of each batch showed in table 2 (Vinay Pandit, 2010).

Evaluation of post-compression parameters

Thickness

The Thickness of the tablets was determined using a Screw guage.

Weight Variation Test

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance and the test was performed according to the official method. Weight Variation limits as per USP.

Hardness

For each formulation, the hardness of 6 tablets was determined using the Monsanto Hardness Tester and the average was calculated and presented with standard deviation.

Friability

A sample of 6 tablets was taken and was carefully dedusted prior to testing. The tablets were accurately weighed and placed in the drum of the Roche Friabilator. The drum was rotated for 100 times at 25 rpm and the tablets were removed, dedusted and accurately weighed.

Table 2: Pre-compression parameters

Formulation code	Compressibility index	Angle of repose	Hausner's ratio
FM 1	12.5	28° 7'	1.15
FM 2	15.9	29° 3'	1.19
FM 3	12.8	27° 5'	1.13
FM 4	15.7	28° 1'	1.17
FM 5	12.4	28° 4'	1.10
FM 6	11.2	27° 9'	1.13
FM 7	12.2	26° 7'	1.16
FM 8	12.3	25° 7'	1.10
FM 9	15.9	29° 3'	1.19
FM 10	12.8	27° 6'	1.13
FM 11	15.7	28° 1'	1.17
FM 12	12.3	28° 4'	1.11
FM 13	11.2	27° 9'	1.13
FM 14	13.4	26° 6'	1.18
FM 15	14.2	27° 6'	1.08
F 1	12.4	28° 4'	1.14
F 2	11.2	27° 9'	1.13
F 3	12.1	26° 7'	1.18

Drug Content

The drug content of the tablet was determined according to within acceptable official limit of 85% to 115%. Ten tablets with pre determined weight from each batch were taken and crushed in a mortar and weight and weight equivalent to one average tablet was taken, transferred to a 250 ml volumetric flask and 0.1 N HCl was added. The flask was kept on mechanical shaker for overnight, later is taken out and volume was made up to 100 ml with 0.1 N HCl. The solution was filtered through a filter paper and the first few ml were discarded. The filtrate was sufficiently diluted and the absorbance was recorded and analyzed in UV spectrophotometer against the blank at 275 nm.

Table 3: Post-compression parameters

Formulation code	Hardness (kgs)	Weight variation (mg)	Thickness (mm)	Friability (%)	Drug content
FM 1	6.1	200.8	3.21	0.65%	99.01%
FM 2	5.8	200.61	3.11	0.71%	101.02%
FM 3	5.6	201.01	3.24	0.81%	98.2%
FM 4	5.4	200.0	3.22	0.89%	97.28%
FM 5	5.1	200.7	3.19	0.91%	99.12%
FM 6	6.1	200.1	3.21	0.47%	102.06%
FM 7	5.9	199.8	3.11	054%	100.07%
FM 8	5.8	199.7	3.17	0.63%	100.01%
FM 9	5.5	200.9	3.23	0.69%	99.01%
FM 10	5.4	200.3	3.10	0.72%	101.2%
FM 11	6.2	200.2	3.20	0.31%	99.87%
FM 12	6.0	199.6	3.18	0.39%	98.02%
FM 13	5.7	199.7	3.16	0.47%	97.29%
FM 14	5.5	199.9	3.14	0.51%	98.76%
FM 15	5.4	199.8	3.12	0.58%	98.66%
F1	6.4	200.7	3.15	0.23%	99.6%
F2	6.8	201.1	3.13	0.22%	99.98%
F3	6.9	200.8	3.10	0.20%	98.28%

Floating Properties of Tablets

The *in vitro* buoyancy was determined by floating lag time. Table 4 shows the results of buoyancy study. The tablets were placed in a 100 ml glass beaker containing 0.1 N HCl. (1) Floating Lag Time: The time required for the tablet to rise to the surface of the medium and float was determined as floating lag time, (2) Floating Duration Time: The time for which the tablet remained floating on the surface of medium was determined as floating duration (Cheueh H R, 1995).

Swelling index

The studies were carried out gravimetrically; Table 4 shows the results of swelling index. Swelling media used for these studies were distilled water and simulated gastric fluid (pH 1.2). The prepared tablets were introduced into the swelling media. At predetermined time intervals the tablets were removed from medium, excess water was blotted with tissue paper and immediately weighed (Belgamwar VS, 2009). This procedure was repeated until the tablet reached constant weight. The swelling index was calculated using following formula,

$$\text{Swelling Index} = W1—WO / WO \times 100$$

Where,

W1=Weight of dry tablet,

W0= Weight of swollen tablet was determined as floating duration time.

***In vitro* Drug Release Studies**

The release rate of drug from floating and Bioadhesive tablets was determined using USP Type 2 Apparatus. The dissolution test was performed in triplicate, using 900ml of 0.1N HCL, at 37± 0.5˚C at 50 rpm for 24 hrs. A 5ml sample was withdrawn from the dissolution apparatus at specified time points and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45-µm membrane filter and diluted if necessary. Absorbance of these solutions was measured at 275nm using U.V-Visible Spectrophotometer. Cumulative drug release was calculated using the equation (y = 0.0238x + 0.000246) generated from Beer Lambert's Calibration curve in the linearity range of 5-50µg/ml (Girish S. Sonar, 2007).

***Ex-vivo* Bioadhesion test for Bioadhesive tablets**

Bioadhesive force measurement of tablets was done by modifying balance method. The right pan was replaced with a glass beaker container and on the left side beaker with a copper wire. Teflon block of 1.5 cm diameter and 3 cm height was adhered strongly with the glass beaker. The two sides were then adjusted, so that the left hand side was exactly 5 gm heavier than the right. Stick the stomach on the Teflon block with help of the cynoacrylate glue and fill the beaker with acidic buffer till the tissue remains in a moist condition. Stick the tablet to beaker and put on the tissue for a 15 minute. After 15 minute add water slowly in to right beaker until the tablet detaches. Weight the water required for the tablet detachment. Calculate Actual weight for detachment and force of adhesion in dyne by following equation (Belgamwar VS, 2009; Girish S. Sonar, 2007).

Drug release kinetic models

To describe the kinetics of the drug release from tablet, mathematical models such as zero-order, first order, Higuchi, and Korsmeyer-Peppas models were used. The

Table 4: Floating properties and Swelling index

Formulation	Floating Lag Time (sec)	Floating Time (hrs)	Swelling Index
FM 1	19	18	120%
FM 2	18	16	107%
FM 3	16	16	93%
FM 4	14	15	82%
FM 5	13	15	75%
FM 6	39	>24	149%
FM 7	30	>24	127%
FM 8	24	23	101%
FM 9	20	23	91%
FM 10	19	22	81%
FM 11	107	>24	162%
FM 12	104	>24	149%
FM 13	83	>24	133%
FM 14	80	>24	109%
FM 15	79	>24	97%
F1	32	>24	130%
F2	41	>24	159%
F3	74	>24	181%

Table 5: cumulative % drug release of Glipizide Floating and Bioadhesive tablets

Time (hrs)	0.5	1	2	3	4	6	8	10	12	15	18
FM 1	22.1	36.8	54.8	75.4	81.3	97.1	-	-	-	-	-
FM 2	20.3	29.4	50.4	59.6	74.8	92	-	-	-	-	-
FM 3	19.4	29.7	48.7	55.6	72	86.1	-	-	-	-	-
FM 4	16.8	25.8	36.5	49.8	67.7	85.1	-	-	-	-	-
FM 5	10.7	22.1	28.2	56.1	64.1	75.1	-	-	-	-	-
FM 6	14.8	22.7	29.6	45.9	59.5	74.7	83.4	92.1	95.4	-	-
FM 7	12.9	20.8	33.7	41.6	63.2	68	79.5	85.8	96.4	-	-
FM 8	15.4	23.3	28.7	38.6	52.5	66.3	75.1	81.6	89.9	-	-
FM 9	10.3	18.8	26.7	48.6	51	63.9	72.1	79.2	86.6	-	-
FM 10	8.1	16.2	22.5	36.8	48.1	60.8	68.4	75.8	79.9	-	-
FM 11	11	18.9	24.6	35.7	41	49.2	54.4	65.1	67.1	72.2	75.6
FM 12	9.7	21.2	26.5	34.6	38.3	46.3	50.4	57.3	62	66.5	70.9
FM 13	8.9	15.3	23.1	36	37.1	45.4	49.6	55.9	58.9	64.2	66
FM 14	7.7	14.7	19.7	27	33.1	44.4	48.4	53.4	58.1	63.9	64.8
FM 15	7	13.5	19.2	30	36.6	39.3	42.5	44	52.5	56.3	57.6
F 1	20.6	38.8	62.8	71.4	89.3	98	-	-	-	-	-
F2	18.8	26.7	35.8	59.7	65.5	79.7	94.4	94.6	96.9	-	-
F3	12.5	22.1	28.9	38.7	44.5	59.2	70.4	77.2	85.2	94	95.9

criterion for selecting the most appropriate model was chosen on the basis of the goodness-or fit test (Mukhopadhyaya S, 2010).

Stability studies

The optimized tablets from batch FM 8 were charged for stability studies. There was no change in physical appearance, color. Formulations were analyzed at the end of Three months for the assay and dissolution studies. Average drug content of the tablets were found to be 98.5±0.6% of the labeled claim. In vitro dissolution profile showed that there was no significant change in the release rate of the drug from optimized tablets at the end of three months.

RESULTS AND DISCUSSION

All formulation was done by direct compression technique. Out of FM1 to FM15 batches Table 2, 3 shows the results of FM8 trial was selected on the basis of linearity and accuracy in performance characteristic (pre-compression & post-compression). Table 4 shows the results of buoyancy study, it was clearly observed that the reduction in concentration of HPMC in each batch the floating lag time increased as well as floating duration decreased. And also increase in viscosity of HPMC polymers delayed the floating lag time and prolonged the drug release. Table 4 shows the results of swelling index, all formulations of Glipizide Floating Bioadhesive drug delivery tablets were evaluated for

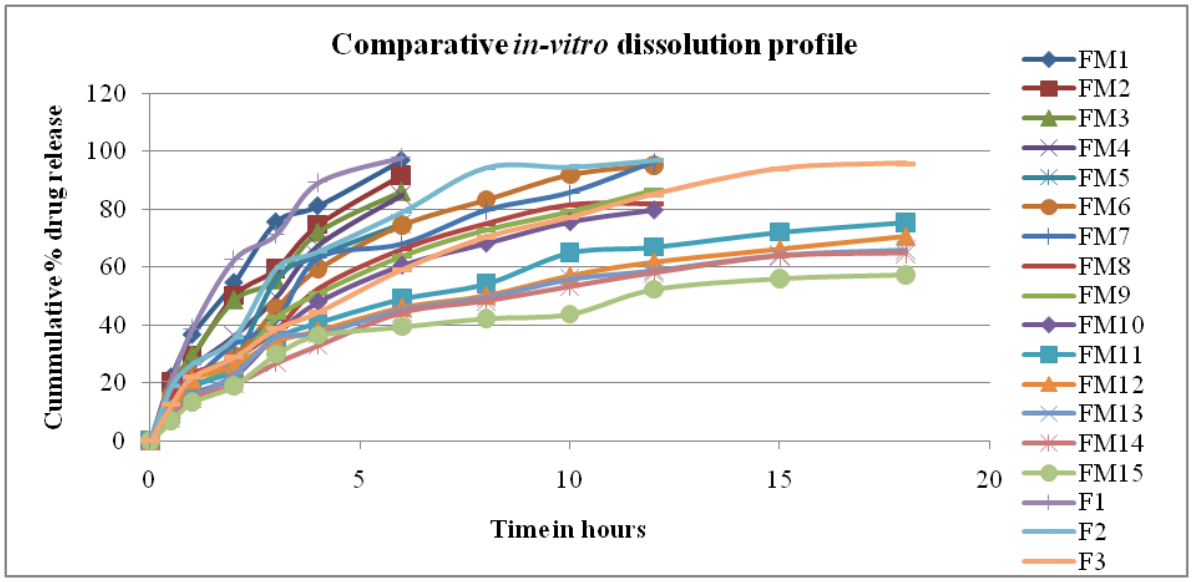

Figure 4: Comparative in vitro dissolution profile

Table 6: Bioadhesive strength (n=3) of all formulations

Formulation code	Bioadhesion Strength (gm)	Force of adhesion (N) in dyne
FM1	17.1±0.29	1.67
FM2	18.5±0.47	1.81
FM3	19.3±0.16	1.89
FM4	20.1±0.37	1.97
FM5	22.5±0.15	2.20
FM6	21.4±0.37	2.09
FM7	24.2±0.46	2.37
FM8	26.6±0.31	2.60
FM9	28.2±0.42	2.76
FM10	29.6±0.25	2.90
FM11	43.6±0.21	4.27
FM12	44.2±0.36	4.33
FM13	45.4±0.27	4.45
FM14	48.2±0.16	4.72
FM15	51.6±0.31	5.06
F1	9.4±0.28	0.92
F2	10.1±0.52	0.99
F3	15.6±0.22	1.53

water uptake study. And it was concluded that as the viscosity of hydrophilic polymer concentration increases the water uptake increase which results in increasing of swelling index. At the same time concentration of HPMC also has similar impact on the swelling property of the formulation. Table 5 & Figure 4 shows the results of *In- vitro* drug release data and profiles, drug release of Glipizide floating Bioadhesive tablets (n=3) formulated with HPMC K4M. Formulations FM 1 to FM 5 are composed with HPMC K4M as a hydrophilic polymer and a Bioadhesive polymer Carbopol 974P, in increasing ratios of Carbopol and decreasing ratios of hydrophilic polymer. Formulation F 1 is composed without Bioadhesive polymer, which is designed to find out the difference in drug release rate compared to floating and Bioadhesive tablets. Here the effect of concentration of hydrophilic polymer to Carbopol is observed. The decrease in concentration of HPMC retards the drug release from formulation. This may be expected due to the increase in concentration of Carbopol 974P which is having high molecular weight as well as more drug release retarding property compared to that of HPMC K4M. There is no much difference in drug release was observed with formulations of FM 1 – FM 5 to that of F1 which has no Bioadhesive polymer .Drug release of Glipizide floating Bioadhesive tablets (n=3) formulated with HPMC K15M. Formulations FM 6 to FM 10 are composed with HPMC K15M as a hydrophilic polymer and a Bioadhesive polymer Carbopol 974P, in increasing ratios of Carbopol and decreasing ratios of hydrophilic polymer. Formulation F 2 is composed without Bioadhesive polymer, which is designed to find out the difference in drug release rate compared to floating and Bioadhesive tablets. Here the

Table 7: Drug kinetic release of Glipizide Floating and Bioadhesive tablets

Formula code	Zero order	First order	Higuchi	Korsmeyer Peppas	
	R^2	R^2	R^2	R^2	n
FM1	0.933	0.817	0.986	0.988	0.603
FM2	0.970	0.872	0.995	0.995	0.621
FM3	0.962	0.860	0.991	0.993	0.606
FM4	0.985	0.919	0.979	0.989	0.655
FM5	0.900	0.825	0.955	0.965	0.802
FM6	0.943	0.815	0.987	0.986	0.625
FM7	0.928	0.778	0.981	0.984	0.637
FM8	0.932	0.882	0.992	0.525	0.571
FM9	0.936	0.771	0.990	0.985	0.671
FM10	0.929	0.762	0.984	0.981	0.729
FM11	0.924	0.765	0.988	0.987	0.549
FM12	0.916	0.716	0.985	0.963	0.520
FM13	0.892	0.709	0.975	0.972	0.571
FM14	0.933	0.763	0.991	0.987	0.612
FM15	0.874	0.683	0.958	0.957	0.586
F1	0.926	0.773	0.978	0.972	0.634
F2	0.927	0.817	0.981	0.981	0.585
F3	0.965	0.814	0.997	0.995	0.588

effect of concentration of hydrophilic polymer to Carbopol is observed. The above graph shows that, the decrease in concentration of HPMC retards the drug release from formulation. This may be expected due to the increase in concentration of Carbopol 974P which is having high molecular weight as well as more drug release retarding property compared to that of HPMC K15M. There is no much difference in drug release was observed with formulations of FM 6 – FM 10 to that of F 2 which has no Bioadhesive polymer in its formulation. Drug release of Glipizide floating Bioadhesive tablets (n=3) formulated with HPMC K100M. Formulations FM 11 to FM 15 are composed with HPMC K100M as a hydrophilic polymer and a Bioadhesive polymer Carbopol 974P, in increasing ratios of Carbopol and decreasing ratios of hydrophilic polymer. Formulation F 3 is composed without Bioadhesive polymer, which is designed to find out the difference in drug release rate compared to floating and Bioadhesive tablets. Here the effect of concentration of hydrophilic polymer to Carbopol is observed. The above graph shows that, the decrease in concentration of HPMC retards the drug release from formulation. This may be expected due to the increase in concentration of Carbopol 974P which is having high molecular weight as well as more drug release retarding property compared to that of HPMC K100M. There is no much difference in drug release was observed with formulations of FM 11 – FM 15 to that of F 3 which has no Bioadhesive polymer in its formulation. Table 6 shows the results *ex-vivo* bioadhesive strength, this evaluation test was conducted for all formulations. There is a gradual increase in Bioadhesion strength was observed in each batch i.e., from FM1 to FM5, FM 6 to FM 10 and FM11 TO FM 15. This is due to the increase in concentration of Bioadhesive polymer Carbopol 974P. But compared to the formulations F1, F2, and F3, all the above formulations shown the good Bioadhesive property because F1, F2, and F3 contains no Bioadhesive polymer. Here the study investigates the Bioadhesive properties of formulations from FM1 to FM15. The maximum Bioadhesion strength 43.6g, 44.2g, 45.4g, 48.2g, 51.6g was found for formulations FM11 to FM 15 respectively. And low Bioadhesion strength 17.1g, 18.5g 19.3g, 20.1g, 22.5g was found for Formulations FM1 to FM5. This may be expected that as the viscosity of the hydrophilic polymer increases the adhesive property is also increases. The formulations FM11 to FM15 were made up of HPMC K100M which is of greater viscosity compared to HPMC K4M and HPMC K15M. Table 7 shows the results drug kinetic release, It was found out that the optimized formulation was best explained by the Higuchi's equation, as the plots showed highest linearity (R^2 = 0.992) with diffusion.

CONCLUSION

Among these formulations with HPMC K100M shown controlled release, but complete drug release is not observed. Hence it was concluded that the formulations with K15M is optimized for better release. FM8 formulation is optimized among the K15M Formulations because of its equal combination of bioadhesive polymer and hydrophilic polymer. Major disadvantage of floating system is requirement of a sufficient high level of fluids in the stomach for the drug delivery to float. The floating drug delivery systems are effective only when the fluid level in the stomach is sufficiently high. However, as the stomach empties and the tablet is at the pylorus, the buoyancy of the dosage form may be impeded. This serious limitation can be overcome

by making the floating system eventually adhere to the mucous lining of stomach wall. Thus Floating and bio-adhesive Drug Delivery System (FBDDS), thus, offers the advantage of increased gastric residence time of drugs over normal floating DDS. The FBDDS was successfully formulated by incorporating bioadhesive polymers to normal floating drug delivery systems.

ACKNOWLEDGEMENT

The authors wish to thanks the Principal Prof. Y. Haribabu I place on record my gratitude to Mr. P. Siva, Mr. Sajeeth C.I., Dr. K. Santhi, Patil Dinesh and management of Grace College of Pharmacy, Kerala for continuous support, encouragement and excellent facilities.

Very special thanks to the management of Bright labs, Hyderabad group for gift samples of drug and providing excellent research facilities.

REFERENCES

Alexander Streubel. Drug Delivery to the upper small intestine window using Gastroretentive technologies, current option in pharmacology. 2006: 6:501 – 508.

Belgamwar V S, S J surana. Floting bioadhesive drug delivery system using novel effervescent agents, Asian j. pharm, apr- june, 156-160, 2009.

Cheueh H R, H Zia, C T Rhodes. Optimization of sotolol floating and bioadhesive extended release tablet formulations, drug delivery and Indian pharm., 1995, 21(15), 1725-1747.

Girish S. Sonar, Devendra K. Jain, Dhananjay M. More. "Preparation and in vitro evaluation of bilayer and floating-bioadhesive tablets of rosiglitazone maleate", Asian Journal of Pharmaceutical Science, 2007, 2 (4), 161-169,

Mukhopadhyaya S, Goswami, Satheesh madhav NV, Upadhyaya K. formulation and evaluation of floating bioadhesive tablets of ciprofloxacin hydrochloride by direct compression technique, int. j. pharmacy and pharm.sci., vol 2, 3, 113-115, 2010.

Vinay Pandit, Hemant Joshi, Sarasija Suresh. Gastro retentive drug delivery system of Amoxycillin, International Journal of Pharma and bio sciences v1 (2) 2010.