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GLIPIZIDE LOADED FLOATING MICROSPHERE: FORMULATION AND EVALUATION

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ABSTRACT

Purpose: The aim of the present investigation was to formulate and evaluate the gastro-retentive floating drug delivery system of glipizide (as microsphere), that would retain the drug in stomach and continuously release the drug in controlled manner up to a predetermined time leading to improved bioavailability. **Methods:** In the present investigation eight formulations of glipizide were prepared as the floating microspheres using hydroxypropylmethylcellulose (HPMC) and eudragit RS100 polymers. **Results:** The densities of floating microspheres (0.475-0.975 gm/cm^3) were found to be less than the density of gastric fluid (1.004 gm/cm^3), therefore showed an extended floating time of more than 12 h over the gastric fluid. The percentage entrapment efficiency of prepared floating microspheres was 76.19 - 41.32%. The scanning electron microscopy confirmed the hollow nature of microspheres with pores on the surface of floating microspheres, which imparted floating properties to the prepared floating microspheres. F4 formulation shows the greater entrapment efficiency in the range of (64.76 %) with the ratio of drug: polymer (HPMC: Eudragit RS 100) (1:4:3). F4 formulation shows good *in-vitro* release with (99.12 %) in 12 h in 0.1 N HCl. The kinetic study of prepared floating microspheres showed controlled drug release by matrix diffusion Process with zero order release rate kinetics. **Conclusion:** The formulated gastro retentive floating drug delivery systems of glipizide showed good physicochemical properties, good stability and controlled drug release pattern, thereby improving the bioavailability of the drug and also manage the complicacy of the diabetes in a better manner.

KEYWORDS: Floating microspheres, Glipizide, HPMC (hydroxypropylmethylcellulose).

INTRODUCTION

Diabetes is one of the major causes of death and disability in the world. The latest, WHO estimate for the number of people with diabetes worldwide, in 2000, is 171 million, which is likely to be at least 366 million by 2030. The focus of medical community is on the prevention and treatment of the disease, as is evident from the rising number of research papers every year on the subject.[1]

Floating Drug Delivery Systems (FDDS) or Hydrodynamically Balanced Systems (HBS) are among the several approaches that have been developed in order to increase. The gastric residence time (GRT) of dosage forms .Both single and multiple unit Systems have been developed .The single-unit floating systems are more popular but Have a disadvantage owing to their' all-or-nothing' emptying process leading to high Variability of the gastro intestinal transit time .Still, the multiple-unit dosage forms may be better suited because they are claimed to reduce the inter subject variability in absorption and lower the probability of dose dumping. Such a dosage form can be distributed widely through out the gastrointestinal tract (GIT), affording the possibility of a longer lasting and more reliable release of the drug from the dosage form.[2]

Drugs that are easily absorbed from the gastrointestinal tract (GIT) and have a short half-life are eliminated quickly from the blood circulation, so they require frequent dosing. To avoid this drawback, the oral sustained-controlled release formulations have been developed in an attempt to release the drug slowly into the GIT and maintain an effective drug concentration in the serum for longer period of time. However, such oral drug delivery devices have a physiological limitation (Soppimath et al., 2001) of gastric retention time (GRT), Variable and short gastric emptying time can result in incomplete drug release from the drug delivery system (DDS) in the absorption zone (stomach or upper part of small intestine), leading to diminished efficacy of the administered dose (Chueh et al., 1995; Iannuccelli et al., 1998). To overcome these limitations, approaches being proposed to prolong the GRT include: floating drug dosage systems (FDDS) (Whitehead et al., 2000; Goole et al., 2007; Streubel et al., 2003; Sungthongjeen et al., 2006), swelling or expanding systems (Deshpande et al., 1996, 1997), mucoadhesive systems (Santus et al., 1997), high-density systems (Rouge et al., 1998), modified-shape systems (Kedzierewicz et al., 1999), and other delayed gastric emptying devices.[3]

Floating drug delivery is of particular interest for drugs that (1) act locally in the stomach, (2) are primarily absorbed in the stomach, (3) are poorly soluble at an alkaline pH, (4) have a narrow window of absorption, and (5) are unstable in the intestinal or colonic environment. 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).[4]

Microspheres have been widely accepted as a means to achieve oral and parenteral controlled release drug delivery system. The microsphere requires a polymeric substance as a carrier and a core material. Among the various methods developed for formulation of microspheres, the solvent evaporation method has gained much attention due to its ease of fabrication without compromising the activity of drug. Eudragit ® RS 100 and Eudragit® RL 100 are referred to as ammoniomethacrylate copolymers, with the former having 5% functional quaternary ammonium groups and the latter having 10% functional quaternary ammonium groups. Eudragit® RS 100 is a water-insoluble polymer that is widely used as a wall material for sustained release microcapsules. This is due to its biocompatibility, good stability, easy fabrication and low cost.[5]

The drug of choice, glipizide, is an effective anti -diabetic drug particularly in Type II diabetes (Non-insulin dependent diabetes mellitus). It is a second generation sulfonylurea that actually lowers the blood glucose level in human by stimulating the pancreatic cell and thereby releasing the insulin. It has a short biological half-life of 2 -5 h, which make it more suitable to be designed as a controlled release formulation. The main purpose of the present research was to develop a controlled drug delivery system of glipizide for per-oral administration using biocompatible Eudragit® polymers in order to increase its biological half- life and to determine the influence of formulation and preparation variables on microparticles characteristics, such as drug incorporation and *in-vitro* drug release.

Glipizide is a new second-generation oral hypoglycemic agent that belongs to the sulfonylurea class of compounds. Glipizide is widely used in the management of type II (non-insulin-dependent) diabetes mellitus and like other sulphonylureas. The predominant mechanism of action of glipizide appears to be by increasing the secretion of insulin from the pancreas in both normal and diabetic patients. Other proposed mechanisms include: increasing sensitivity of peripheral tissues to insulin effects, increasing the number of insulin receptors, and increasing binding to and/or affinity of insulin for its receptors. Although sulfonylurea vary widely in their rate of intestinal absorption, the absorption of some drugs

(particularly glipizide) is affected by food. Therefore, glipizide is most effective when given at least 30 min before meals. The usual initial dose of glipizide is 5 mg once or twice daily with a maximum daily divided dose of 40 mg. Peak glipizide blood levels are usually reached within 2 to 4 h after oral administration. Glipizide has a half-life of 2 to 5 h with duration of action of about 10 h. Glipizide has an apparent volume of distribution of 0.16 L/kg, is extensively metabolized in the liver, and 68% to 85% of the given dose is excreted unchanged or as inactive metabolites in urine. Most commonly encountered side effects of sulfonylurea include: nausea, vomiting, headache, weakness, and, rarely, hypoglycemia and coma. These side effects are less common with glipizide treatment.[6]

MATERIALS AND METHODS

MATERIALS

The polymer Eudragit RS 100 and HPMC was purchased from the Ponmani labs, Coimbature (India). The anti-diabetic drug glipizide supplied as a gift sample by Micro labs, Hosur (India). All other chemicals were of analytical reagent grade and were used as received.

METHODS

PREPARATION OF FLOATING MICROSPHERES[7]

Floating microsphere containing glipizide was prepared using emulsion solvent diffusion technique. The drug to polymer ratio used to prepare the different formulations was 1:7. The polymer content was a mixture of Eudragit RS 100 (ES 100) Hydroxypropylmethylcellulose (HPMC). The drug polymer mixture was dissolved in a mixture of ethanol (8 ml) and dichloromethane (8 ml). The mixture was dropped in to 0.75% polyvinyl alcohol solution (200 ml). The solution was stirred with a propeller-type agitator at 40° C for 1 h at 300 rpm. The formed floating microspheres were passed through sieve no.-12 and washed with water and dried at room temperature in a desiccator. (Table 1)

CHARACTERIZATION OF MICROSPHERES

Particle size analysis[8-10]

Particle size analysis plays an important role in determining the release characteristics and floating property. The sizes of floating microspheres were measured by using an optical microscope, and the mean particle size was calculated by measuring nearly 200 particles with the help of a calculated ocular stage micrometer.

Floating behaviour of hollow microsphere[11]

100 mg of the hollow microsphere were placed in 0.1 N HCl (300 ml) containing 0.02% Tween 20. The mixture was stirred with paddle at 100rpm. The layer of buoyant microballoons was pipetted and separated by filtration at 1, 2, 4 and 6 h (Table 2). The collected microballoons were dried in a desiccator over night. The percentage of microballoons was calculated by the following equation.

$$\% \text{ hollow microsphere} = \frac{\text{Weight of hollow microsphere}}{\text{Initial weight of hollow microsphere}} \times 100$$

Drug entrapment[12]

The various formulations of the hollow microspheres were subjected for drug content. 50 mg of hollow microspheres from all batches were accurately weighed and crushed. The powdered of microspheres were dissolved with 10ml ethanol in 100ml volumetric flask and makeup the volume with 0.1 N HCl. This resulting solution is then filtered through whatmann filter paper No. 44. After filtration, from this solution 10 ml was taken out and diluted up to 100 ml with 0.1 N HCl. Again from this solution 2 ml was taken out and diluted up to 10 m1 with 0.1 N HCl and the absorbance was measured at 276 nm against 0.1 N HCl as a blank. (Table 2)

Determination of true density[8-9]

The true density of floating microspheres was determined by liquid displacement method using n-hexane as solvent. A pycnometer was used to determine true density. First of all weight of pycnometer (a) was noted and then 25 ml of n-hexane was added and weight (b) was noted. The pycnometer was emptied and weight amount of floating microspheres was added net weight was noted (c). Now n-hexane was added to occupy the void spaces within the floating microspheres untill and floating microspheres n-hexane together occupied the volume i.e. 25ml. Again weight (d) was noted and then true density was calculated according to following formula.

$$\text{Density of liquid (p)} = \frac{b-a}{25}$$

$$\text{True density} = \frac{c-a}{25-\left[\frac{d-c}{\rho}\right]}$$

Determination of tapped density[9]

It is the ratio between a given mass of hollow microspheres and its volume after tapping. Tapped density of hollow microspheres was determined by the tapping method. Accurately weighed quantity of hollow microspheres was transferred in to a 10 ml measuring cylinder. After observing the initial volume of floating micro spheres, the tapping was continued on a hard surface until no further change in volume was noted and the tapped density was calculated.

Percentage Compressibility Index[9]

The same tapping method was used to determine percentage compressibility index.

Percentage Yield[7]

The percentage yield of different formulations was determined by weighing the hollow microspheres after drying. The percentage yield was calculated as follows.

$$\% \text{ Yield} = \frac{\text{Total weight of hollow microspheres}}{\text{Total weight of drug and polymer}} \times 100$$

Angle of repose[9]

Flow property of hollow microspheres is usually assessed by determining angle of repose of the floating micro spheres. It is the maximum angle that can be obtained between the free floating surface of floating micro balloons heap and the horizontal plane. The angle of repose of hollow microspheres was determined by fixed funnel method. The hollow microspheres were allowed to fall freely through a funnel until apex of conical pile just touched the tip of the funnel.

The angle of repose ϕ was determined according to the following formula

$$\phi = \tan^{-1} h/r$$

Where, h = height of pile r = radius of the pile formed by the hollow microspheres.

Shape and surface characterization of hollow microspheres by scanning electron microscopy

From the formulated batches of floating microspheres, formulations (F_4) which showed an appropriate balance between the buoyancy and the percentage release were examined for surface morphology and shape using scanning electron microscope JEOL, JSM-670F Japan (Sastra university, Tanjavur).

Sample was fixed on carbon tape and fine gold sputtering was applied in a high vacuum evaporator. The acceleration voltage was set at 3.0KV during scanning. Microphotographs were taken on different magnification and higher magnification (500X) was used for surface morphology. (Fig. 1)

Fourier transform infra-red spectroscopy (FT-IR) analysis[13]

The Fourier transform infra-red analysis was conducted for the analysis of drug polymer interaction and stability of drug during formulation process. Fourier transform infra-red spectrum of pure glipizide, eudragit RS 100, HPMC, physical mixture and floating microspheres (formulation) were recorded.

***In-vitro* release studies[7]**

The drug release rate from floating microspheres was carried out using the USP type II (Electro Lab.) dissolution paddle assembly. A weighed amount of floating microspheres equivalent to 100 mg drug were dispersed in 900 ml of 0.1 N HCl (pH 1.2) maintained at 37 ± 0.5°C and stirred at 100 rpm. One ml sample was withdrawn at predetermined intervals and filtered and equal volume of dissolution medium was replaced in the vessel after each withdrawal to maintain sink condition. The collected samples were suitably diluted with 0.1 N HCl and analyzed spectrophotometrically at 276 nm to determine the concentration of drug present in the dissolution medium. The dissolution studies were repeated using phosphate buffer pH 6.8 as dissolution medium.

Drug release kinetic data analysis[14-16]

Several kinetic models have been proposed to describe the release characteristics of a drug from matrix. The dissolution profile of all the formulations was fitted to Zero order, Higuchi, Korsemeyer-Peppas to ascertain the kinetic modeling of drug release.

The value of 'n' gives an indication of the release mechanism. When n = 1, the release rate is independent of time (typical zero order release / case II transport); n = 0.5 for Fickian release (diffusion/ case I transport); and when 0.5 < n < 1, anomalous (non-Fickian or coupled diffusion/ relaxation) are implicated. Lastly, when n > 1.0 super case II transport is apparent. 'n' is the slope value of log M_t/M_∞ versus log time curve.

In-vivo anti-diabetic study[17]

In-vivo evaluation studies for glipizide floating microspheres were performed on normal healthy Wistar rats weighing 250 to 300 g each. The approval of the Institutional Animal Ethics Committee was obtained before starting the study (NCP/IAEC/PG/08/2008-2009). The study was conducted in accordance with standard institutional guidelines. Two groups of Wistar rats (5 in each group) that were fasted (with water) at least 12 h before the experiments were used for the study. Before drug administration, a blood sample as a control was taken from each rat from behind the eyeball through the angle of ocular cavity using small capillary tubes. The blood glucose level for the control and test samples was determined using the glucose-measuring instrument glucometer.

The instrument was self-calibrated, and the samples were allowed to dry before the results were read to avoid contamination of the lens. Pure glipizide and floating microspheres of glipizide were administered orally to each group using stomach intubations. A dose of 800 mg/kg of glipizide was administrated in a suspension form (freshly prepared) for each rat. Blood samples were collected at predetermined time at 1-h intervals up to 24 h, and the blood glucose level was performed as per method described earlier. The percentage reduction in blood glucose level was measured.

Stability Study[15, 16]

From the prepared floating microspheres F_4 which showed appropriate balance between the buoyancy and the percentage release was selected for stability studies. The prepared formulation (F_4) were placed in borosilicate screw capped glass containers and stored at different temperature (27 ± 2° C), oven temperature (40±2° C) and in refrigerator (5-8° C) for a period of 90 days. The samples were assayed for drug content at regular intervals of two week. (Table 3)

RESULTS AND DISCUSSION

Particle size was determined by Optical microscopy method. If size of microballoons is less than 500 µm release rate of drug will be high and floating ability will reduce, while microballoons ranging between 500µm - 1000µm, the floating ability will be more and release rate will be in sustained manner. In the present study hollow microsphere of Glipizide was prepared by emulsion–solvent diffusion method by using Eudragit RS100 and HPMC as a polymer. The Mean particle size of the microspheres significantly decrease with increase in the concentration of HPMC and was in the range from 609 to 874 µm, due to change in drug and polymer ratio.

Drug entrapment of all formulation was found in range of 41.32 to 76.19% w/w and its efficiency slightly decreases with increasing the HPMC content. When the distribution coefficient was high efficiency of drug entrapment into microballoons was elevated. This phenomenon was due to the lack of retention of drugs with low distribution coefficient in the emulsion droplet aqueous solution during the process, which led to reduced entrapment of drug into microballoons.

True density, tapped density values for all formulation were less than that of gastric fluid (1.004 gm/cm^3) suggested that it exhibit good buoyancy. Buoyancy of the microballoons decreased with increasing drug release. The floating ability pattern differed according to the formulation tested and medium used. F4 gave the best floating ability in all media, as evidenced by the percentage of particles floated at different time intervals. This can be mainly due to its low bulk density value obtained before and after tapping, respectively. All formulations showed excellent flowability as represented in the terms of angle of repose (<40°), due to the polymer ratio. Angle of repose in range of (25^0.39'-37^0.72') all formulation showed excellent flow ability.

Shape of the hollow microsphere was found to be spherical by SEM study; small cavity were present on surface, which may be due to solvent evaporation during drying process, the microspheres floated for prolonged time over the surface of the dissolution medium without any apparent gelation, which is responsible for floating property. SEM Surface morphology of formulation F4 exhibited a smooth surface of the floating microballoons. (Fig. 1)

In FTIR study, all characteristic peaks were appeared in hollow microsphere spectra with out any remarkable change in the position after successful formulation. Hence, it infers that there

is no chemical interaction between the drug and polymers used in the preparation of floating microspheres. FT-IR Spectra of Glipizide, Eudragit RS 100, HPMC, physical mixture of drug polymer and F4 formulation were recorded. The Glipizide present in the formulation F4 was conformed by FTIR spectra. The characteristic peaks due to pure Glipizide at 3250.16, 2943.47, 1689.70, 1651.12, 1373.36, 1159.26, 686.68 for N-H stretching, C-H Stretching, C= O Stretching, -CONH- Stretching, C-H bending, S=O Stretching, C-H Bending respectively, which were shown in Table 4. All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Glipizide and polymer. It also confirmed the stability of drug during the process.

Ideal property of hollow microspheres includes high buoyancy and sufficient release of drug in pH 1.2. Percentage drug release for the formulations F_1, F_2, F_3 (43.791%, 56.311%, 78.809%) in 12 h, is slow and incomplete drug release. In order to increases the percentage drug release, the ratio of Eudragit and HPMC is decreased and increased respectively. F_5, F_6 formulations showed high release rate (94.681%, 97.348%) in 10 h and F_7, F_8 formulations showed high release rate (96.295%, 95.329%) in 9 h, with less buoyancy. F_4 formulation showed appropriate balance between buoyancy and drug release rate of 94.68% in 12 h, which is considered as a best formulation.

Drug release pattern was evaluated in 0.1 N HCl (Fig.2). Release rate of F_1, F_2, F_3 formulations were found to be slow and incomplete in both dissolution medium. It was found that drug release rate increased by decreasing and increasing the ratio of Eudragit and the HPMC respectively. Kinetics and mechanism of drug release from all formulation was evaluated on the basis of zero order, Higuchi equation and Peppas model (Table 3). Correlation coefficient (r^2) and slope value for each equation in the range of 0.752-0.937 and 0.568-0.785, respectively, for Peppas model. Zero order plots for all formulations were found to be linear in acidic and buffer solution of pH 1.2. Which indicates that it may follow zero order kinetics.

Higuchi plot was found to be linear, which indicates diffusion may be the mechanism of drug release for each formulation. Peppas plot was found with good linearity, its $n > 0.5$ for all formulations, indicating that drug release may follow anomalous diffusion (range=0.993-0.998).

Zero order plots for F_4 formulation was found to be linear in both dissolution medium, and is considered as a best fit for drug release. That indicates it may follow zero order mechanism. The *in-vitro* release data was applied to various kinetic models to predict the drug release kinetic mechanism.

Stability study was carried out for the F4 formulation by exposing it to different temperature 5-8°C, 27°C and 40°C for 3 months. The sample was analyzed for drug content at the regular intervals. In stability study, there was no remarkable change in content of F4 formulation during 90 days in which it was stored at various temperatures.

In-vivo efficiency of the optimized batch F_4 was performed in healthy normal Wistar rats by measuring the hypoglycemic effect produced after oral administration. The drug was administered at a dose equivalent to 800 mg/kg pure glipizide, and glipizide floating microspheres were used for the study. Pure glipizide drug was administered in a suspension form at the same dose. When pure glipizide suspension was administered, a rapid reduction in blood glucose levels was observed (Table 5) and maximum reduction of 42.83% was observed within 2 h after oral administration. Blood glucose levels were recovered rapidly to the normal level within 8 h. In the case of glipizide floating microspheres, the reduction in blood glucose levels was slow and reached maximum reduction of 41.16 within 4 h after oral administration. This reduction in blood glucose levels was sustained over longer periods of time (12 h). Kahn and Shechter have suggested that a 25% reduction in blood glucose levels is considered a significant hypoglycemic effect. Significant hypoglycemic effect (25%) was maintained only from 0.5 to 5 h after oral administration of glipizide, whereas in the case of glipizide floating microspheres, significant hypoglycemic effect (25%) was maintained for a period of 2 to 12 h. The hypoglycemic effect observed over a longer period of time in the case of floating microspheres is due to the slow release and absorption of glipizide over longer periods of time. Glipizide formulation is significantly more effective than the immediate release formulation of glipizide in reducing fasting plasma glucose levels and side effects. So the F4 formulation signifies that the hypoglycemic activity of the optimized formulation is decreased when compared to pure drug. Significant hypoglycemic effect (25%) was maintained only from 0.5 to 5 h after oral administration of glipizide, whereas in the case of glipizide floating microspheres, significant hypoglycemic effect (25%) was maintained for a period of 2 to 12 h.

Table 1: FORMULATION OF FLOATING MICROSPHERES

Sr. No	Formulation Code	Glipizide (gm)	Eudragit Rs 100 (gm)	HPMC (gm)
1	F_1	0.1	0.7	0.0
2	F_2	0.1	0.6	0.1
3	F_3	0.1	0.5	0.2
4	F_4	0.1	0.4	0.3
5	F_5	0.1	0.3	0.4
6	F_6	0.1	0.2	0.5
7	F_7	0.1	0.1	0.6
8	F_8	0.1	0.0	0.7

Table 2: PERCENTAGE BUOYANCY FOR DIFFERENT FORMULATION

Formulation	Percentage buoyancy after 6 h	Drug entrapment (% w/w)*
F_1	91.47	76.19 ± 1.2
F_2	87.34	70.59 ± 0.5
F_3	78.45	66.23 ± 1.3
F_4	72.97	64.76 ± 1.1
F_5	66.12	61.01 ± 0.9
F_6	57.76	57.38 ± 1.1
F_7	45.09	48.47 ± 0.8
F_8	36.18	41.14 ± 0.6

*Average of three.

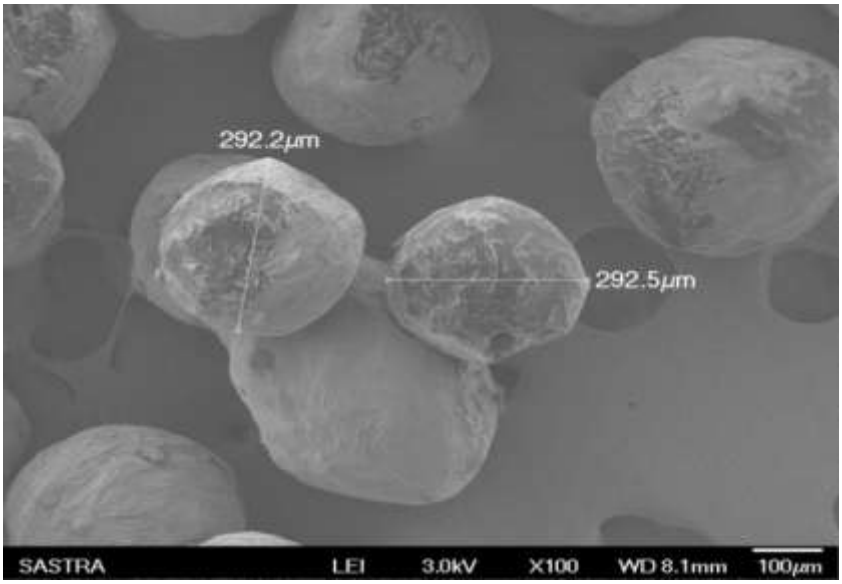

Fig 1: MICRO PHOTOGRAPHS OF FORMULATION F_4

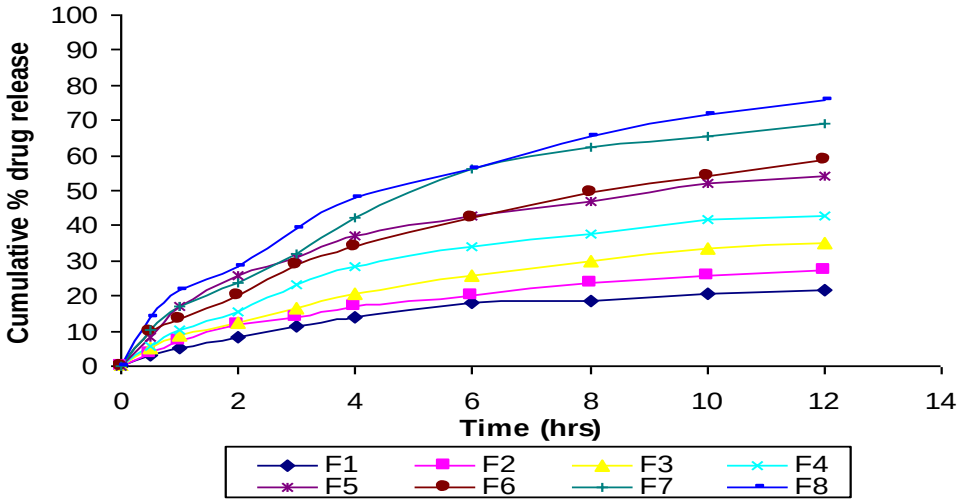

Fig. 2. *In-vitro* drug release in 0.1 N HCl

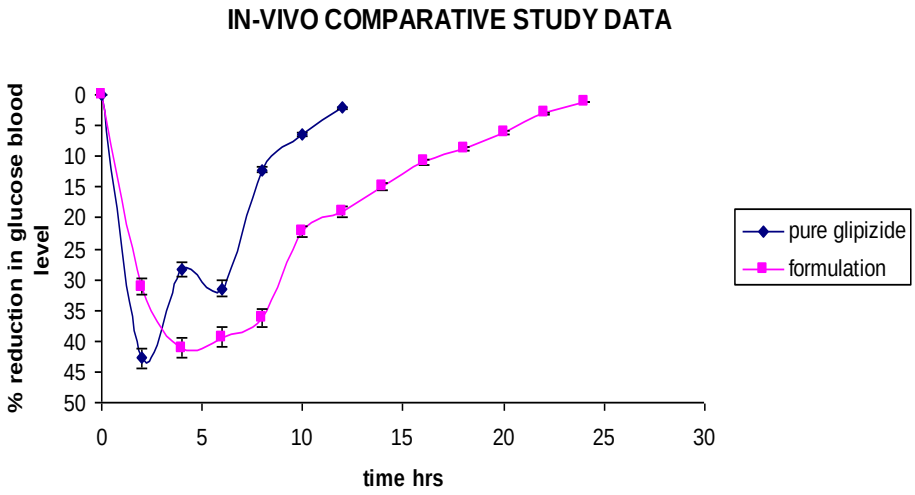

Fig 3: IN-VIVO RELEASE STUDY OF THE DRUG GLIPIZIDE AND THE FORMULATION

Table 3. RELEASE KINETICS OF HOLLOW MICROSPHERE IN 0.1 N HCl

Formulation	Zero Order		Higuchi Equation		Peppas Equation	
	r^2	K_0	r^2	K_H	r^2	n
F_1	0.950	1.81	0.989	6.946	0.937	0.756
F_2	0.954	2.08	0.998	8.141	0.817	0.785
F_3	0.963	2.86	0.994	11.04	0.872	0.769
F_4	0.948	3.49	0.996	13.66	0.835	0.634
F_5	0.930	4.03	0.993	16.09	0.752	0.664
F_6	0.964	4.68	0.996	18.08	0.822	0.612
F_7	0.956	5.80	0.998	22.42	0.833	0.581
F_8	0.954	5.85	0.997	22.86	0.759	0.568

TABLE 4: FT-IR SPECTRUM RANGES

S. No.	Transition	Ranges (cm^{-1})	Drug	Physical Mixture	Formulation
1.	N-H str	3000-3700	3250.16	3251.13	3251.13
2.	C-H str	2700-3300	2943.47	2944.44	2923.22
3.	C=O str	1650-1700	1689.70	1689.70	1688.73
4.	-CONH- str	1650-1700	1651.12	1650.16	1651.12
5	C-H bend (Cyclohexane)	1345-1450	1373.36	1374.33	1384.94
6	S=O str	1149-1180	1159.26	1160.22	1137.07
7	C-H bend (Benzene)	650-900	686.68	686.68	686.68

Table 5: RESULT OF ANTI -DIABETIC ACTIVITY MEASUREMENT

S. No.	Time (h)	Pure Glipizide (% reduction)	Formulation(F_4) (% reduction)
1	0	0	0
2	2	42.83	31.16 ± 4.54
3	4	28.33	41.16 ± 5.73
4	6	31.5	39.33 ± 5.62
5	8	12.16	36.16 ± 4.91
6	10	6.33	22.16 ± 6.13
7	12	2.16	19.00 ± 4.74
8	14	-	14.83 ± 2.83
9	16	-	10.83 ± 3.76
10	18	-	8.83 ± 2.77
11	20	-	6.16 ± 1.92
12	22	-	3.00 ± 0.82
13	24	-	1.16 ± 0.27

CONCLUSION

Drug absorption in the GIT is a highly variable process, prolonging gastric retention of the dosage forms and extends the time of drug absorption. Floating hollow microspheres are prepared with enteric coated polymer (Eudragit RS 100) successfully by the solvent evaporation technique. Upon incorporation of the hydrophilic polymer such as HPMC in the shell of microballoons, the amount of drug released from microspheres could be enhanced. *In-vitro* data obtained from floating microspheres of Glipizide showed excellent floatability, good buoyancy and prolonged drug release. Microspheres of different size and drug content could be obtained by varying the formulation variables. Diffusion (Anamolous transport diffusion) was found to be the main release mechanism. Thus the prepared floating microspheres may prove to be potential candidates for multiple-unit delivery devices adaptable to any intra gastric condition.

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