

FORMULATION AND OPTIMISATION OF GASTRO RETENTIVE DRUG DELIVERY SYSTEM CONTAINING GLIPIZIDE

DAS SAUMYA, PATTANAYAK DHARMAJIT*

Department of Pharmaceutics, Vikas College of Pharmaceutical Sciences, Rayanigudem, Suryapet, Nalgonda, A.P. 508376
Email: dharmajit.pattanayak@gmail.com

Received: 12 Feb 2011, Revised and Accepted: 18 May 2011

ABSTRACT

The purpose of this investigation was to prepare a gastro retentive drug delivery system of Glipizide. Floating tablets of Glipizide were prepared employing Eudragit and two different grades of Hydroxy Propyl Methyl Cellulose K4M (HPMCK4M) and Hydroxy Propyl Methyl Cellulose K100M (HPMCK100M) polymers by effervescent technique. Sodium bicarbonate was incorporated as a gas-generating agent. The Floating tablets were evaluated for uniformity of weight, hardness, friability, drug content, *in vitro* buoyancy and dissolution studies. The drug release profile and floating properties was investigated. The prepared tablets exhibited satisfactory physico-chemical characteristics. All the prepared batches showed good *in vitro* buoyancy. The tablets showed good results for *in-vitro* buoyancy studies and floating time. It was observed that the tablets remained buoyant for 18-20 hours. The tablets with an optimum concentration of HPMCK4M and HPMCK100M were found to float for longer duration and showed maximum drug release as compared to other formulations containing mixture of HPMC and Eudragit.

Keywords: Glipizide, Floating tablets, *in-vitro* buoyancy, HPMC, Eudragit

INTRODUCTION

The bioavailability of drugs with an absorption window in the upper small intestine is generally limited with conventional pharmaceutical dosage forms. The residence time of such systems and, thus, of their drug release into the stomach and upper intestine is often short¹. To overcome this restriction and to increase the bioavailability of these drugs, controlled drug delivery systems, with a prolonged residence time in the stomach, can be used. Incorporation of the drug into a CR-delivery system, which releases its payload in the stomach over a prolonged time period, can lead to significant therapeutic advantages owing to various pharmacokinetic (PK) and pharmacodynamic aspects².

Glipizide is a second-generation sulfonylurea that can acutely lower the blood glucose level in humans by stimulating the release of insulin from the pancreas and is typically prescribed to treat type II diabetes (non-insulin-dependent diabetes mellitus)³. Its short biological half-life necessitates that it be administered in two or three doses of 2.5 to 10 mg per day.

Glipizide is available in a Gastrointestinal Therapeutic System (GITS) extended-release formulation. Glipizide GITS provides more stable plasma drug concentrations than the immediate release formulation and the once-daily regimen may optimize patient compliance. In

patients with type II diabetes mellitus, glipizide GITS is at least as effective as the immediate-release formulation of glipizide in providing glycaemic control, and may have a greater effect on fasting plasma glucose levels⁴.

MATERIALS AND METHODS

Material

Glipizide was obtained as gift sample from Micro laboratories, Bangalore. Polyvinyl pyrrolidone (PVP) and sodium lauryl sulfate (SLS) was obtained from Loba Chemie, Pvt, Ltd, Mumbai. Hydroxypropyl methylcellulose (HPMC) of 4000 CPS viscosity and Eudragit RS100 were purchased from Merck Chemicals Ltd. Germany. Other reagents and solvents were of analytical grade.

Preparation of Gastro Retentive Controlled Release Tablets.

Glipizide was mixed with the required quantities of Lactose, HPMCK4M, HPMCK100M, Eudragit and Sodium bicarbonate by geometric mixing after that the mixture was blended with magnesium- stearate and further mixed for additional 2-3 minutes. Then the powder was compressed on tablet punch machine with 8mm dia. The weight of the tablets was kept constant for formulations F1 to F9. The composition of all formulations was given in (table.1)

Table 1: Formulation Table

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Glipizide	10	10	10	10	10	10	10	10	10	10
HPMCK4M	30	-	-	10	10	20	-	-	10	20
HPMCK100M	-	30	-	10	20	10	10	20	-	-
Eudragit	-	-	30	10	-	-	20	10	20	10
Sod. Bicarbonate	20	20	20	20	20	20	20	20	20	20
Talc	1	1	1	1	1	1	1	1	1	1
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2
Lactose DC	97	97	97	97	97	97	97	97	97	97

Note: All quantities are in mg. Total weight of each tablet is 160mg.

Evaluation of Powder Blend

Bulk density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A suitable amount of powder from each formulation, previously lightly shaken to break any agglomerates formed, was

introduced into a 10 ml measuring cylinder. After initial volume was observed, the cylinder was allowed to fall under its own weight on to a hard surface from a height of 2.5cm at 2 seconds intervals. The tapping was continued until no further change in volume was noted. LBD and TBD were calculated.

Evaluation of tablets

Two tablets from each formulation were randomly selected and organoleptic properties such as colour, odour, taste, and shape were evaluated. Thickness and diameter of ten formulations were measured using vernier calipers. Five tablets from each formulation were used and average values were calculated. Hardness of the tablets was tested using Monsanto hardness tester for each formulation. The friability of the tablets was determined using Roche Friabilator. From each formulation six tablets were subjected to the test. Under weight variation test, 20 tablets were selected randomly from each formulation and weighed individually using an electronic balance to check the weight variations as per U.S. Pharmacopoeia.

In-vitro Buoyancy Studies

Duration of buoyancy lag time and floating time were observed. The in-vitro buoyancy was determined by floating lag time. The tablets were placed in 100ml beaker containing 100ml 0.1N HCl. The time required for the tablets to rise to the surface and float was determined.

Drug Content Estimation

Five tablets were taken and amount of drug present in each tablet was determined as follows: Tablets were crushed in mortar and transferred to 100 ml flask. The powder was dissolved in 3 ml of methanol and volume was made up with 0.1N HCl. The sample was mixed by using Remi mixer for 5 minutes, after which it was filtered through Whatman filter paper. The filtered solutions after appropriate dilution (1 ml to 10 ml) with 0.1N HCl were analyzed by validated UV spectrophotometric method at 276nm.

In Vitro dissolution studies

The dissolution study was carried out in 0.1N HCl using USP dissolution test apparatus employing basket stirrer. In this study, one tablet containing 10 mg of glipizide was placed inside the 900 ml dissolution medium and speed of basket was set at 75 rpm. Samples were (5 ml) withdrawn at a time interval of 1 hour and same volume of fresh medium was replaced. The samples were analyzed for drug content against 0.1N HCl as a blank at 276nm. The percentage drug release was plotted against time to determine the release profile.

RESULTS AND DISCUSSION

The floating tablets of Glipizide were prepared by effervescent technique using HPMC K4M, HPMCK100M, Eudragit and sodium bicarbonate. The magnesium stearate and lactose were used as lubricant and glidant, respectively. The bulk density and angle of repose showed that the flow properties of the powder blend of different formulations were found to be satisfactory. The variation in weight was within the range of $\pm 5\%$ complying with pharmacopoeia specifications. The hardness for different formulations was found to be between 5-6 kg/cm² indicating satisfactory mechanical strength. The friability was below 1% for all the formulations, which is an indication of good mechanical resistance of the tablets. The drug content for all the formulations were found to be in the range of 92.94% to 101.52%. The buoyancy lag time was in the range of 36s to 61s. The floating time of the formulations containing high percentage of HPMCK100M was less as compared to remaining formulations. All the formulations showed controlled release kinetics. Formulations showed release in the range of 39.12% to 71.28%. Formulations containing more concentration of HPMCK100M showed slow controlled release. Formulations containing Eudragit showed less release due to rate controlling polymer. Formulation F5 showed a release of 71.28% in 12hrs due to optimum percentage of HPMCK4M and HPMCK100M.

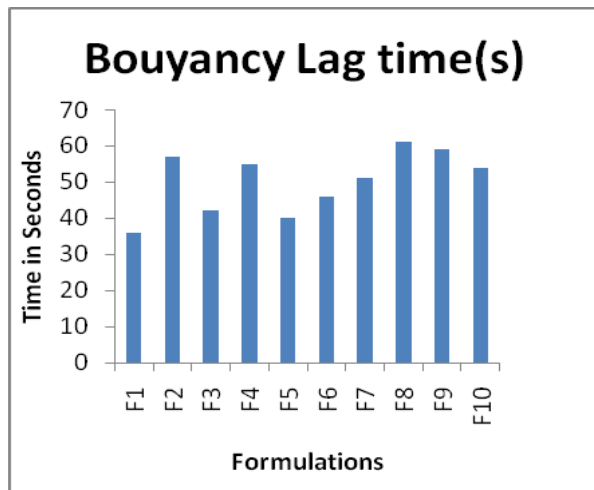


Fig. 1: Buoyancy lag time

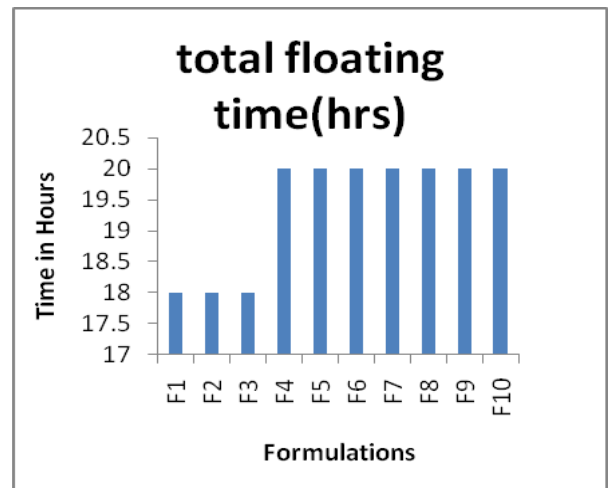


Fig. 2: Floating time

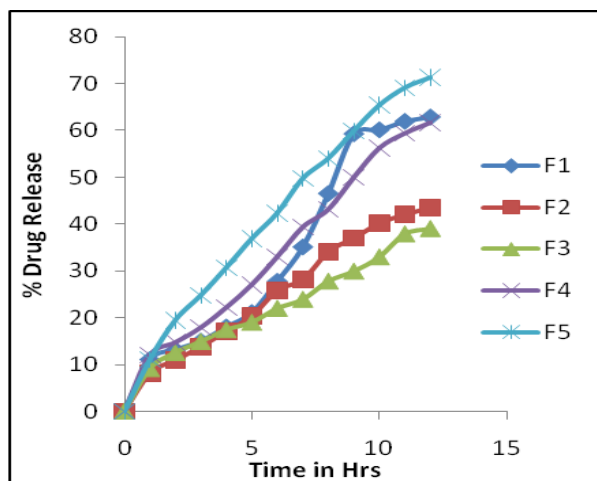


Fig. 3: % Drug Release of Formulations F1 to F5

CONCLUSION

From the results it was concluded that all formulations showed a controlled release pattern. But formulation F5 was optimised due to its high percentage of release in 12hrs. Other parameters like floating time, buoyancy lag time, etc showed satisfactory results for formulation F5. Thus it was concluded that an effective floating drug delivery system can be designed using various grades of HPMC.

REFERENCES

- Alexander Streubel, "Drug Delivery to the upper small intestine window using Gastroretentive technologies", current opinion in pharmacology, 6:501 – 508, 2006.
- Sanjay Garg and Shring Sharma, "Oral Drug Delivery", business Briefing Pharmatech. 2003.
- Shahla Jamzad, Reza Fassihi, "Development of a controlled release low dose class II drug-Glipizide", International Journal of Pharmaceutics 2006; 312, 24–32.
- Jayvadan K. Patel, Rakesh P. Patel, Avani F Amin and Madhabhai M. Patel, "Formulation and Evaluation of Mucoadhesive Glipizide Microspheres", AAPS PharmSciTech 2005; 6 (1) Article 10 331-337.
- Patil J M, Hirlekar R S, Gide P S and Kadam V J, "Trends in floating drug delivery systems", Journal of sci. and Ind. Res. jan 2006; Vol-65, 11-21.

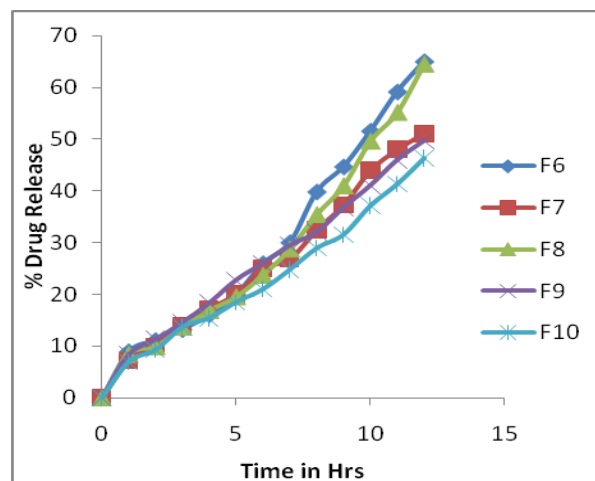


Fig. 4: % Drug Release of Formulations F6 to F10

- Jaleh Varshosaz, N Tavakoli and F Roozbahani, "Formulation and invitro characterization of ciprofloxacin floating and bioadhesive extended release tablets", drug delivery 2006;Vol-13: 277-285.
- Rajan K. Verma, Sanjay Garg "Development and evaluation of osmotically controlled oral drug delivery system of Glipizide", European J. Pharm. and Biopharm. 2004; 57, 513–525.
- Davis S S. "Formulation strategies for absorption windows", Drug Discovery Today 2005; 10, 249-256.
- Garg R, Gupta G D. "Progress in controlled gastroretentive delivery systems", Tropical journal of pharmaceutical research 2008; 7(3), 1055-1066.
- Radhikaa P R, Pala T K, Sivakumar, "Formulation and Evaluation of Sustained Release Matrix Tablets of Glipizide", Iranian Journal of Pharmaceutical Sciences 2009; 205-214.
- B. Seshagiri, Dr. K.A. Chowdary, Y Deepthi Priya, Formulation and evaluation of sintered gastro retentive tablets of Glipizide; International Journal of Pharmacy and Pharmaceutical Sciences 2011; Vol-3, Suppl 4; 128-135.
- Praveena Nasa, Sheefali Mahant, Deepika Sharma, "Floating systems: a novel approach towards gastroretentive drug delivery systems", International Journal of Pharmacy and Pharmaceutical Sciences 2010; Vol-2, Suppl 3, 1-7.