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Sustained Release Gastroretentive Beads Of Glipizide: A Novel Drug Delivery Approach For Enhanced Glycemic Control

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Abstract

The present study focuses on the development and evaluation of sustained release gastroretentive floating beads of Glipizide to enhance gastric residence time and improve oral bioavailability for effective type 2 diabetes management. Glipizide, a second-generation sulfonylurea, is characterized by a short biological half-life and site-specific absorption in the upper gastrointestinal tract, making it an ideal candidate for gastroretentive drug delivery systems. Floating beads were prepared using ionotropic gelation with a blend of polymers including Hydroxypropyl Methylcellulose (HPMC K4M), Carbopol, Eudragit RL-100, and Sodium Alginate, with calcium chloride serving as the crosslinking agent. The formulations were evaluated for drug-polymer compatibility using Fourier-transform infrared spectroscopy (FTIR), and assessed for buoyancy behavior, entrapment efficiency, particle morphology, swelling index, and in vitro drug release. Among the various formulations, the optimized batch demonstrated excellent floating capacity (more than 12 hours), high drug entrapment efficiency (>85%), and sustained release over a 10-hour period. Drug release followed non-Fickian diffusion as indicated by Higuchi and Korsmeyer-Peppas kinetic models. The study concludes that gastroretentive floating beads of Glipizide provide a promising controlled-release system that may improve glycemic control, reduce dosing frequency, and enhance patient compliance. Further in vivo studies are recommended to substantiate these in vitro findings and confirm clinical applicability.

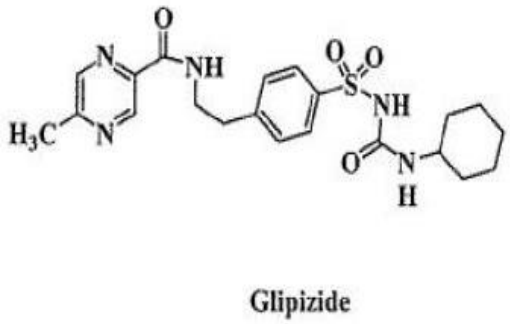
Key words: Glipizide, Floating beads, Sustained release, Carbopol

1. Introduction

Diabetes mellitus is a chronic metabolic disorder that continues to pose a significant public health challenge worldwide. It is characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both[1]. Type 2 diabetes mellitus (T2DM) is the most prevalent form, often linked to sedentary lifestyles, obesity, and genetic predisposition. Uncontrolled diabetes leads to serious complications such as nephropathy, retinopathy, neuropathy, and cardiovascular diseases, necessitating sustained glycemic control through effective therapeutic strategies[2].

Glipizide, a second-generation sulfonylurea, is widely prescribed for the treatment of T2DM. It promotes insulin secretion from pancreatic β-cells but suffers from a short biological half-life (2–5 hours) and limited absorption in the upper gastrointestinal tract[3]. These pharmacokinetic drawbacks necessitate multiple daily dosing, reducing patient compliance and therapeutic consistency[4].

Gastroretentive drug delivery systems (GRDDS) offer a novel approach to address these limitations by prolonging gastric residence time and improving the absorption window[5]. Floating beads represent a promising GRDDS platform, especially for drugs like Glipizide. Polymers such as Hydroxypropyl Methylcellulose (HPMC K4M), Carbopol, and Eudragit RL-100 can be utilized to provide controlled drug release and sustained buoyancy[6]. This study aims to formulate Glipizide-loaded floating beads using ionotropic gelation, evaluate their physicochemical properties, and investigate their potential to enhance therapeutic efficacy and patient adherence in T2DM management[7-14].



Glipizide

Figure 1 : Chemical Structure of Glipizide

2. Materials and Methods

Materials

Glipizide, Hydroxypropyl Methylcellulose (HPMC K4M), and Carbopol were procured from Biocon Biopharmaceuticals, India. Sodium Alginate and Calcium Chloride (analytical grade) were obtained from Sigma-Aldrich. Eudragit RL-100 was supplied by Nice Chemicals, Cochin, India. All reagents used were of analytical grade and used as received without further purification.

Preparation of Floating Beads

Glipizide-loaded floating beads were prepared using the ionotropic gelation technique. Calculated amounts of HPMC K4M, Carbopol, and Eudragit RL-100 were individually dissolved in distilled water and stirred using a magnetic stirrer for 2 hours. Sodium Alginate was dissolved separately in distilled water to form a homogenous solution. Glipizide was added to the polymer solution and ultrasonicated for 5–10 minutes to ensure uniform dispersion and to remove entrapped air bubbles.

The drug-polymer dispersion was then dropped via a syringe fitted with a 21-gauge needle into 100 mL of 10% w/v Calcium Chloride solution under gentle agitation. The formed beads were allowed to cure in the gelation medium for 15–25 minutes to complete cross-linking. The beads were collected, washed with distilled water to remove surface $CaCl_2$, and dried at 60°C in a hot air oven for 24 hours.

Evaluation of Beads

Beads were evaluated for percentage yield, drug content, entrapment efficiency, swelling index, in vitro buoyancy, and in vitro drug release using USP Type II dissolution apparatus in 0.1 N HCl (pH 1.2) at 37±0.5°C. Samples were withdrawn at regular intervals and analyzed spectrophotometrically at 276 nm.

Drug–Polymer Compatibility Study

Fourier-transform infrared (FTIR) spectroscopy was performed using KBr pellet technique to detect any potential interaction between Glipizide and the excipients used.

Kinetic Modeling of Drug Release

The release data were fitted into various kinetic models including zero-order, first-order, Higuchi, and Korsmeyer-Peppas equations to determine the mechanism of drug release from the floating beads.

3. Results and Discussion

The Glipizide-loaded floating beads were successfully formulated using ionotropic gelation with various combinations of polymers. All the batches (F1–F7) exhibited uniform shape and good structural integrity. The visual inspection confirmed that the beads were spherical and robust with no signs of aggregation.

FTIR spectroscopy revealed no significant shifts or disappearance of characteristic peaks in the spectra of drug-polymer mixtures compared to the pure drug, indicating no chemical interaction and confirming compatibility among Glipizide and excipients.

Entrapment efficiency ranged from 76.5% to 89.6%, with the highest observed in formulation F5, which contained a balanced ratio of HPMC K4M, Carbopol, and Eudragit RL-100. This increase can be attributed to the synergistic gel-forming and viscosity-enhancing effects of the polymers, which effectively trapped the drug within the matrix.

In vitro buoyancy studies showed that all formulations floated immediately or within 35 seconds of contact with gastric fluid and maintained buoyancy for more than 12 hours, which is essential for prolonged gastric residence. Formulation F5 showed the shortest floating lag time (20 seconds), supporting its suitability for sustained gastroretention.

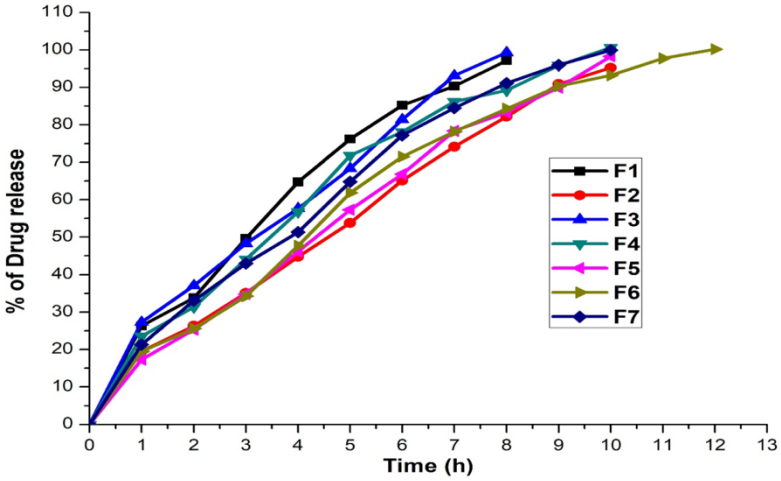
In vitro drug release profiles demonstrated sustained Glipizide release over a 10-hour period across all formulations. F5 again showed optimal performance, releasing approximately 90.8% of the drug gradually, minimizing the risk of dose dumping. The release kinetics were evaluated using various mathematical models. The best fit was obtained with the **Higuchi model** (R^2 = 0.9942), suggesting diffusion as the dominant release mechanism. Additionally, the **Korsmeyer–Peppas model** (R^2 = 0.9865) indicated anomalous (non-Fickian) transport, which involves a combination of diffusion and erosion processes.

These findings suggest that F5 is an optimized formulation offering a balance of high entrapment, sustained release, and excellent buoyancy. The enhanced performance is likely due to the combined effect of hydrophilic matrix formation and mucoadhesive properties of the selected polymers, supporting the goal of a gastroretentive system that improves Glipizide bioavailability and therapeutic consistency.

Table 1: Post-compression parameters for Glipizide floating beads formulation F1-F7

Formulation	Percentage yield (%)	Drug content (%)	pH	Viscosity(cps)	Swelling index
F1	98.84±0.59	97.47±1.66	5.98±0.78	530.99±1.89	86.88
F2	97.32±0.21	99.11±0.33	6.13±0.98	599.34±11.04	82.87
F3	96.95±1.09	96.11±0.72	6.82±0.72	428.68±17.77	68.82
F4	96.77±0.32	96.99±0.43	6.43±0.11	460.77±15.42	77.22
F5	97.91±0.14	96.11±0.34	6.11±1.32	472.75±13.82	84.32
F6	98.81±0.12	97.59±0.23	6.7±0.83	566.96±10.21	78.91
F7	96.98±0.93	98.56±1.99	6.82±0.01	454.72±13.26	68.11

Figure 2: In vitro drug release of Glipizide floating bead (Formulations F1-F7)



4. Conclusion

The present study successfully developed a sustained-release gastroretentive bead formulation of Glipizide using the ionotropic gelation technique. Among the various polymeric combinations tested, formulation F5—comprising HPMC K4M, Carbopol, Eudragit RL-100, and Sodium Alginate—demonstrated optimal performance in terms of entrapment efficiency, buoyancy, and sustained drug release. FTIR analysis confirmed the absence of drug–excipient interactions, ensuring formulation stability. The in vitro release profile followed Higuchi and Korsmeyer-Peppas models, indicating a diffusion-controlled mechanism with non-Fickian transport. These floating beads showed excellent gastroretentive properties, enabling prolonged residence in the stomach and consistent drug release over 10 hours. This formulation approach offers significant promise for improving the bioavailability and therapeutic efficacy of Glipizide, potentially enhancing glycemic control and patient compliance in the treatment of type 2 diabetes. Further in vivo studies are warranted to validate the clinical applicability of this novel delivery system.

References:

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2013;36(Suppl 1):S67–S74.
2. Deshmukh VN, Sakarkar DM, Purohit AP. Development and evaluation of sustained release micropellets of Glipizide. Indian J Pharm Sci. 2009;71(2):120–3.
3. Patil JM, Hirlekar RS, Gide PS, Kadam VJ. Trends in floating drug delivery systems. J Sci Ind Res. 2006;65:11–21.

4. Menon TV, Sajeeth CI. Formulation and evaluation of carvedilol loaded mucoadhesive microbeads. Int J Pharm Sci Res. 2013;4(2):712–8.
5. Maji R, Tapaswi R, Ray S. Formulation and evaluation of sustained release microspheres of Metformin hydrochloride. Int J Pharm Sci Res. 2012;3(3):852–8.
6. Chowdhury JA, Das MK. Design, development and in vitro evaluation of sustained release alginate beads of Diclofenac sodium. Asian J Pharm Clin Res. 2011;4(3):147–53.
7. Singh A, Sharma R, Garg G. Review: Floating drug delivery system–a novel approach. Int J Pharm Sci Res. 2010;1(2):1–13.
8. Dhanaraju MD, Bhaskar K, Nappinnai M. Formulation and evaluation of sustained release microspheres of Diclofenac sodium using sodium alginate. J Pharm Sci Res. 2009;1(4):64–71.
9. Giri TK, Alexander A, Tripathi DK, Ajazuddin. Current status and future perspectives on gastroretentive drug delivery systems. Pharm Biol Eval. 2014;1(1):1–13.
10.Vaishnaw HD, Sharma A. Design and evaluation of sustained release matrix tablets of Metformin hydrochloride using natural polymers. Int J Res Pharm Biomed Sci. 2015;6(2):104–10.
11. Majeti NVK. Microparticulate systems for delivery of proteins and peptides. Crit Rev Ther Drug Carrier Syst. 2000;17(5):509–55.
12.Mandal S, Mandal SK. Development of sustained release matrix beads of Trimetazidine dihydrochloride using sodium alginate. Trop J Pharm Res. 2010;9(3):283–91.

13. Samyuktha Rani B, Lakshmi PK. Formulation and evaluation of controlled release mucoadhesive microbeads of Metformin hydrochloride. Int J Pharm Pharm Sci. 2012;4(3):156–62.
14. Roy A, Saha S, Ghosh B. Formulation and evaluation of sustained release matrix tablets of Metformin hydrochloride using HPMC. Int J Curr Pharm Res. 2012;4(3):61–5.