REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 2 (2024)
http://www.veterinaria.org
Article Received: Revised: Accepted:

Formulation And Evaluation of Floating Drug Delivery System of Poorly Water Soluble Drug Glipizide

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Introduction-

Floating tablets are a type of gastro-retentive drug delivery system designed to enhance the retention time of dosage forms in the stomach. By prolonging gastric residence, these systems improve the bioavailability of drugs that have a narrow absorption window, exhibit poor solubility in the alkaline environment of the small intestine, or degrade in the intestinal or colonic regions. The key objective in developing oral controlled-release formulations is not merely to extend drug release beyond 12 hours but to ensure the dosage form remains in the stomach or upper gastrointestinal tract until the drug is completely released over the intended duration. Floating tablets are specially formulated to stay buoyant in gastric fluids, enabling a gradual and uniform release of the drug. This characteristic makes them particularly beneficial for medications that require localized or sustained action in the stomach or upper digestive tract. The advancement of floating tablet technology has become a key focus in pharmaceutical research due to its potential to enhance drug delivery and therapeutic effectiveness. These tablets remain in the stomach for an extended period, leading to improved drug absorption, increased bioavailability, and prolonged gastric retention. The principle behind floating tablets involves incorporating agents that promote buoyancy, such as gas-generating compounds or hydrocolloids. Effervescent agents react with gastric fluids to produce carbon dioxide, enabling the tablet to float, while hydrocolloids, including polymers and gelling agents, expand or form a gel-like barrier upon hydration, further aiding flotation. This buoyant nature offers several benefits, primarily ensuring a controlled and sustained release of the drug, helping maintain consistent therapeutic levels in the stomach [1,2].

Floating tablets are especially beneficial for drugs that are either unstable in the stomach's acidic environment or require localized effects. Additionally, they enhance drug absorption by maintaining prolonged contact with the stomach's absorptive surfaces. Another advantage is improved patient compliance, as these tablets provide sustained drug release, reducing the need for frequent dosing. The development of floating tablets involves careful selection of polymers, gas-generating agents, and excipients, along with optimizing their physical properties and release profile. Various formulation techniques, including direct compression, effervescent systems, and multiparticulate approaches, can be utilized to manufacture these tablets [3, 4].

Preparation of calibration curve of Glipizide in pH buffer

A precisely measured 10 mg of Glipizide was dissolved in 100 ml of freshly prepared 1.2 pH buffer to create a standard stock solution with a concentration of 100 mcg/ml. From this stock solution, aliquots ranging from 0.4 ml to 4.0 ml, corresponding to drug concentrations of 4 to 40 mcg/ml, were taken and transferred into 10 ml volumetric flasks. The volume in each flask was then brought up to 10 ml using the same buffer. The absorbance of all prepared solutions was measured at 276 nm against a blank solution, which was prepared using the same procedure but without the drug. A calibration curve of absorbance versus concentration was then constructed.

Preparation of Glipizide floating tablets

Glipizide floating tablets were formulated using the direct compression technique, incorporating the drug along with varying concentrations of polymers such as HPMC K4M, HPMC K100, and Xanthan gum. Additional excipients included sodium bicarbonate, microcrystalline cellulose (MCC), lactose, magnesium stearate, and talc. The ingredients were thoroughly mixed using a mortar and pestle to ensure uniform blending. Following this, lubrication was carried out with magnesium stearate and purified talc before compressing the mixture into tablets using a tablet punching machine.

Different formulation batches were designed using statistical tools, and an optimized batch was selected for further development. The selection was based on key parameters, including buoyancy lag time (BLT), total floating time (TFT), and in-vitro drug release in a 1.2 pH buffer solution.

Table 1: Composition of Glipizide floating tablets

Ingredients (mg)	F1	F2	F2	F4	F5	F6
Glipizide	10	10	10	10	10	10
HPMC K100	20	25	20	25	30	25
HPMC K4M	25	20	20	25	20	20
Xanthan gum	15	15	20	15	15	20
MCC	50	50	50	50	50	50
Sodium bicarbonate	20	20	20	20	20	20
Magnesium stearate	2	2	2	2	2	2
Talc	3	3	3	3	3	3
Lactose	55	55	55	50	50	50
Total weight	200	200	200	200	200	200

In-vitro drug release study

The dissolution study for all formulations was performed using a USP Type-II dissolution apparatus. A phosphate buffer solution (pH 1.2) with a total volume of 900 mL served as the dissolution medium, maintained at a temperature of 37°C ± 0.5°C and stirred at 50 rpm. At specified intervals, 5 mL aliquots were withdrawn and replaced with an equal volume of fresh dissolution medium. Sampling was conducted at 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, and 12 hours, and the collected samples were analyzed spectrophotometrically at 276 nm.

Drug content

The drug content of Glipizide floating tablets was evaluated. A total of five tablets were finely powdered, and an amount equivalent to 10 mg of Glipizide was precisely weighed and transferred into a 100 ml volumetric flask. The flask was then filled with 0.1N HCl (pH 1.2 buffer solution) and mixed thoroughly. The solution was adjusted to a final volume of 100 ml and filtered. Subsequently, 1 ml of the filtrate was diluted to 10 ml with 0.1N HCl. The absorbance of the resulting solution was then recorded at 276 nm using a Shimadzu UV-visible spectrophotometer.

In-vitro buoyancy studies

The floating behavior of the tablets was evaluated in vitro by immersing them in a 100 ml beaker containing 100 ml of 0.1 N HCl (pH 1.2). The duration taken for the tablet to rise to the surface of the liquid is referred to as the floating lag time (FLT), while the period for which the tablet remains floating continuously on the medium's surface is termed the total floating time (TFT).

RESULT AND DISCUSSION

Glipizide

The current study involved the formulation of floating tablets containing Glipizide, utilizing various viscosity grades of hydroxypropyl methylcellulose (HPMC K4M and HPMC K100) along with Xanthan gum. These formulations demonstrated compatibility with Glipizide, with no signs of physical interaction.

Preparation of Calibration curve of Glipizide

Table 2: Absorbance of different concentrations of Glipizide

Sr. no	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	10	0.198
3	20	0.403
4	30	0.612
5	40	0.804
6	50	0.956

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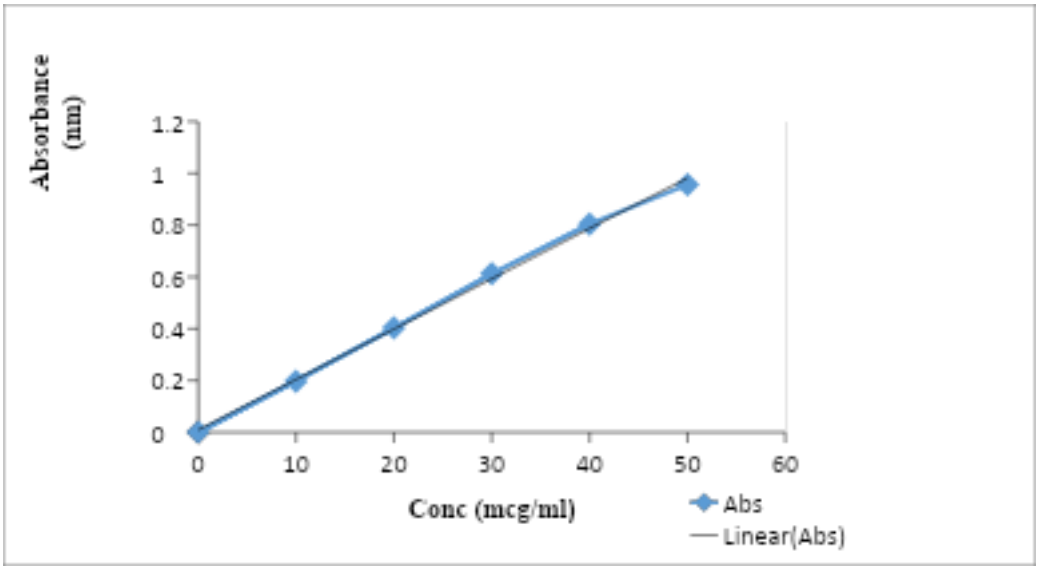

Fig. 1: Calibration Curve of Glipizide

Table 3: Specifications for flow properties

Type of flow	Hausner's Ratio	Angle of Repose	Carr's index
Excellent	1.00-1.11	25-30	<10
Good	1.12-1.18	31-35	11-15
Fair	1.19-1.25	36-40	16-20
Passable	1.26-1.34	41-45	21-25
Poor	1.35-1.45	46-55	26-31
Very poor	1.46-1.59	56-65	32-38
Very, very poor	>1.60	>65	>38

Table 4: Pre-compression parameters of Glipizide floating tablets

Formulation Code	Angle of repose(θ)	Bulk density (gm/cm)	Tapped density (gm/cm)	Hausner ratio	Carr index (%)
F1	27.44	0.221	0.261	1.181	16.398
F2	26.07	0.226	0.261	1.151	16.793
F3	28.47	0.235	0.271	1.191	17.017
F4	**25.65**	**0.251**	**0.267**	**1.107**	**11.707**
F5	29.65	0.231	0.301	1.200	17.677
F6	28.86	0.225	0.263	1.190	15.424

Table 5: Post-compression parameters of Glipizide floating tablets

Formulation Code	Weight variation Average weight in (mg)	Hardness (Kg/cm2)	Thickness in (mm)	Friability (%)	Drug content uniformity (%)
F1	200.26	5.33	3.25	0.80	99.54
F2	200.22	5.86	3.15	0.83	99.46
F3	201.27	5.57	3.20	0.96	99.62
F4	**201.15**	**5.90**	**3.27**	**0.72**	**100.11**
F5	199.29	5.30	3.22	0.85	99.13
F6	200.30	5.35	3.29	0.87	99.37

Table 6: In-vitro buoyancy studies

Formulation Code	Floating lag time FLT (sec)	Total floating time TFT (hrs.)
F1	93	>12
F2	105	>12
F3	123	>12
F4	**65**	**>12**
F5	76	>12
F6	85	>12

The drug powder exhibited an angle of repose ranging from 26.07 to 29.65, while the Carr's index was measured between 11.71 and 15.68, indicating good compressibility of the tablets

Hausner's ratio was determined to be in the range of 2.11 to 2.20, indicating good flow properties. The prepared tablets were assessed for weight variation, and the percentage deviations from the average weight, as presented in Table 6, were found to be within the prescribed official limits.

The friability of the formulations ranged from 0.72% to 0.96%, as shown in Table 6, and remained within the official requirement of not exceeding 1%.

The uniformity of the tablet's thickness suggests consistent die fill. Tablet thickness is influenced by punch size and tablet weight (200 mg). For batches F1 to F6, thickness ranged from 3.15 to 3.289 mm, while hardness was measured between 5.30 and 5.90 Kg/cm², indicating strong mechanical properties. When placed in a 0.1 N HCl solution (pH 1.2) at 37°C, the tablets remained buoyant without breaking apart. Based on the results, batch F4 demonstrated an optimal floating lag time (FLT).

In-vitro dissolution studies were conducted for all tablet batches containing Glipizide using the USP Type II dissolution test apparatus at a speed of 50 rpm. A 900 ml volume of 0.1N HCl served as the dissolution medium. Formulations F1 to F6, composed of the drug and various polymers, underwent in-vitro drug release evaluation over a 12-hour period. The percentage of drug release across different batches ranged from 83.13% to 95.37% within this timeframe. Among them, Formulation F4, incorporating HPMC (K100 & K4), demonstrated complete drug release within 12 hours, making it the optimized formulation with an improved drug release profile.

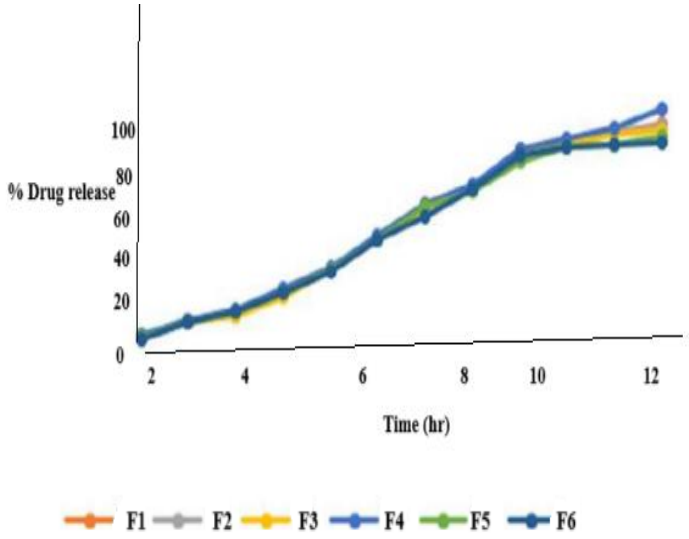

Fig. 2: Dissolution profile of Glipizide floating tablets

CONCLUSION

Glipizide tablets were prepared using the direct compression method. In-vitro buoyancy studies were conducted for all formulations (F1 to F6) in 0.1 N HCl solution at 37°C. Among these, the F4 batch exhibited excellent buoyancy, characterized by a minimal lag time and prolonged floatation exceeding 12 hours in 0.1 N HCl. The in-vitro drug release study was carried out over 12 hours, with the optimized formulation (F4) demonstrating superior drug release compared to the other batches. Based on these findings, F4 is considered a suitable candidate for developing a gastro-retentive floating drug delivery system for Glipizide. The study further highlights that polymer viscosity plays a crucial role in determining the drug release rate and the floating behavior of the tablets.

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