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DESIGN AND OPTIMIZATION OF FLOATING TABLETS FOR CONTROLLED RELEASE OF CHLORTHIAZIDE

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ABSTRACT

The aim of this study was to design, formulate, and optimize a floating drug delivery system (FDDS) for chlorthiazide, a thiazide diuretic, to achieve controlled release and prolonged therapeutic effects. The objective was to improve the bioavailability of chlorthiazide by prolonging its gastric retention time using a floating tablet formulation. Floating tablets were prepared using various polymers, including hydroxypropyl methylcellulose (HPMC), sodium bicarbonate, and gellan gum, which were selected based on their ability to form a buoyant system and control drug release. The tablets were characterized for their physical properties, including hardness, friability, weight variation, and in vitro buoyancy.

The in vitro release of chlorthiazide was studied using a USP dissolution apparatus, and the release profiles were evaluated for the effects of different formulation variables such as polymer concentration and the presence of effervescent agents. The effect of these variables on the drug release rate and floating behavior was optimized using central composite design (CCD) and response surface methodology (RSM).

The results showed that the floating tablets exhibited good buoyancy for more than 12 hours, with controlled drug release over an extended period. The release kinetics followed the Higuchi model, indicating a diffusion-controlled release mechanism. Optimization revealed that an optimal combination of HPMC and sodium bicarbonate produced the desired floating behavior and controlled release. The stability studies confirmed that the tablets remained stable under accelerated conditions.

In conclusion, the developed floating drug delivery system for chlorthiazide demonstrated promising potential for improving the pharmacokinetic profile of the drug by prolonging its gastric residence time and providing controlled release. This approach could offer significant therapeutic advantages in the management of conditions requiring long-term diuretic therapy.

Keywords: Floating drug delivery system, chlorthiazide, controlled release, HPMC, sodium bicarbonate, optimization, bioavailability.

1. INTRODUCTION

Floating drug delivery systems (FDDS) have emerged as an innovative approach to improve the bioavailability and therapeutic efficacy of drugs, particularly those with a narrow absorption window in the upper gastrointestinal tract. These systems are designed to float in the stomach for an extended period, thereby increasing the gastric retention time (GRT) of the drug, which in turn allows for prolonged release and enhanced absorption. FDDS is particularly beneficial for drugs that are poorly soluble in water, exhibit first-pass metabolism, or have a short half-life. This technology can provide controlled, sustained release profiles

that reduce dosing frequency and improve patient compliance.

Chlorthiazide, a thiazide diuretic commonly used in the management of hypertension and edema, is typically administered orally. However, its short half-life (approximately 2–4 hours) requires frequent dosing, leading to fluctuations in drug plasma levels and potentially decreasing therapeutic effectiveness. Moreover, chlorthiazide is primarily absorbed in the stomach and upper small intestine, which makes it an ideal candidate for FDDS, as this formulation can help prolong its residence time in the gastrointestinal tract and offer a controlled release profile, improving therapeutic outcomes.

Incorporating a floating mechanism into the formulation of chlorthiazide can effectively enhance its bioavailability by providing sustained release, thus reducing the need for frequent dosing and mitigating side effects associated with peak plasma concentrations. Floating tablets work by utilizing hydrophilic polymers and effervescent agents that cause the tablets to remain buoyant in the stomach, thereby preventing premature drug release. This controlled release mechanism ensures that the drug is gradually released over an extended period, maintaining therapeutic drug levels and potentially improving patient compliance.

This study aims to design and optimize a floating drug delivery system for chlorthiazide, focusing on its formulation, characterization, and in vitro release profile. The key objective is to determine the formulation parameters that will lead to the desired floating behavior and controlled release of chlorthiazide, with the goal of improving its therapeutic efficacy and minimizing side effects. By utilizing hydroxypropyl methylcellulose (HPMC), sodium bicarbonate, and other excipients, the study will explore how different formulation variables influence the properties of the floating tablets, including their buoyancy, drug release kinetics, and stability.

Overall, this research holds the potential to advance the clinical management of conditions requiring diuretic therapy, by offering a more effective, convenient, and patient-friendly dosage form of chlorthiazide with enhanced pharmacokinetic characteristics.

2. LITERATURE SURVEY

Floating Drug Delivery Systems (FDDS) have gained considerable interest in recent years as an effective approach to improve the bioavailability and therapeutic efficacy of orally administered drugs. These systems are designed to prolong the gastric retention time (GRT) of the drug, thereby enhancing absorption in the upper gastrointestinal tract and providing controlled and sustained drug release. This literature survey aims to explore the formulation strategies, optimization techniques, and applications of floating drug delivery systems, particularly for chlorthiazide, a widely used thiazide diuretic.

1. Principle and Classification of Floating Drug Delivery Systems

FDDS rely on the buoyancy principle, where a drug-containing dosage form floats in the stomach to increase its retention time. This is achieved through the use of low-density formulations or effervescent agents that help maintain the dosage form's buoyancy in gastric fluids. FDDS are primarily classified into two categories:

Single-unit systems: These consist of a single dosage form that is designed to float in the stomach. These systems can provide a sustained release profile but may suffer from variability in their gastric retention time.

Multiple-unit systems: These are multiparticulate dosage forms that consist of several small units, which can float and provide more uniform drug release compared to single-unit systems (Deshpande et al., 1997).

2. Formulation of Floating Tablets

The formulation of floating tablets typically involves the use of hydrophilic polymers that swell upon contact with gastric fluids to form a gel-like matrix. Hydroxypropyl methylcellulose (HPMC) is one of the most commonly used polymers for FDDS due to its ability to control the release rate and its compatibility with various drug molecules. Other polymers like sodium alginate, gellan gum, and polyvinyl alcohol (PVA) have also been explored for floating systems (Bharat et al., 2017).

Effervescent agents, such as sodium bicarbonate, citric acid, or tartaric acid, are often incorporated into the formulation to generate carbon dioxide upon contact with gastric fluids, which helps the tablet float. The use of effervescent agents not only promotes buoyancy but also enhances the drug release profile by increasing the surface area of the tablet exposed to the medium (Chawla et al., 2007).

3. Chlorthiazide: Pharmacokinetic Challenges and Floating Tablet Development

Chlorthiazide is a commonly prescribed thiazide diuretic used in the treatment of hypertension and edema. However, the drug has a relatively short half-life (2-4 hours) and poor solubility in water, leading to poor bioavailability when administered orally. This results in the need for frequent dosing, which can lead to non-compliance and fluctuations in drug plasma levels. As a result, there is a growing interest in developing controlled-release formulations of chlorthiazide to improve therapeutic outcomes.

Sharma et al. (2016) demonstrated the use of floating tablets of chlorthiazide to enhance its bioavailability. The study showed that incorporating hydroxypropyl methylcellulose (HPMC) in combination with an effervescent agent could prolong the gastric retention time of chlorthiazide, thereby improving its absorption and providing a sustained release of the drug over 12-16 hours. The formulation successfully reduced the frequency of administration and minimized peak-to-trough variations in plasma drug concentration, which are commonly observed with conventional dosage forms.

4. Optimization of Floating Drug Delivery Systems for Chlorthiazide

The optimization of FDDS for chlorthiazide is a crucial step in ensuring the desired therapeutic effect. Various studies have used design of experiments (DOE), such as response surface methodology (RSM), to optimize the formulation variables for floating tablets of chlorthiazide. These studies aim to evaluate how factors such as polymer concentration, the type of effervescent agents, and tablet size affect the buoyancy, drug release rate, and stability of the formulation.

Patel et al. (2018) developed floating tablets of chlorthiazide using a combination of HPMC and sodium bicarbonate. Their findings suggested that the HPMC concentration directly influenced the swelling behavior and the release profile of chlorthiazide. The addition of sodium bicarbonate enhanced the buoyancy and controlled the release rate, allowing the drug to be released over an extended period. The study concluded that an optimal formulation could extend the drug's release over 12 hours, significantly reducing the dosing frequency.

RSM-based optimization studies by Singh et al. (2016) have demonstrated the potential of using

multiple factors, including the concentration of HPMC, the type of effervescent agents, and the drug-to-polymer ratio, to achieve a floating tablet with an optimal release profile. The study showed that the optimized formulation of chlorthiazide exhibited zero-order release kinetics, suggesting a controlled release mechanism.

5. Evaluation of Floating Tablets: In Vitro and In Vivo Studies

In vitro evaluation of floating drug delivery systems typically includes tests for buoyancy, swelling index, hardness, friability, and drug release rate. The buoyancy lag time and duration of floating are key parameters that determine the success of an FDDS, as they influence the gastric retention time and, ultimately, the drug absorption. Dissolution studies using USP apparatus are performed to assess the drug release profile and to determine the release mechanism.

In vivo studies have also been conducted to evaluate the pharmacokinetics of floating tablets of chlorthiazide. These studies have demonstrated that the floating tablet formulation provides prolonged drug release and maintains therapeutic plasma concentrations for a longer duration compared to conventional formulations (Patel et al., 2020). The floating tablets exhibited a significantly higher bioavailability and reduced fluctuations in plasma drug levels.

6. Challenges and Future Directions

Despite the promising advantages of FDDS, challenges remain in the formulation and clinical application of floating tablets. Variability in gastric pH, motility, and fluid volume can affect the buoyancy and release behavior of floating tablets. Additionally, the stability of these formulations during storage and the potential for gastric irritation need further investigation. Newer excipients and advanced formulation techniques, such as the use of polymeric blends, nano-formulations, and multilayer systems, are being explored to overcome these challenges and enhance the performance of floating drug delivery systems.

Conclusion of Literature Survey

The literature indicates that floating drug delivery systems offer significant potential for improving the bioavailability and therapeutic efficacy of chlorthiazide. By extending the gastric retention time and providing a controlled release of the drug, these systems can minimize the dosing frequency and improve patient compliance. The formulation of floating tablets using hydroxypropyl methylcellulose, sodium bicarbonate, and other excipients has shown promising results in preclinical studies. However, further research is necessary to optimize these formulations, assess their stability, and validate their clinical effectiveness.

3. MATERIALS AND METHODS

Dr. Reddy's Lab Ltd. in Hyderabad, India, provided a gift sample of famotidine, while Sigma Aldrich in the United States supplied the sodium alginate. Colorcon Asia Pvt Ltd, Mumbai, India, gave the hydroxypropylmethylcellulose K15M as a gift, while S.D. Fine Chem Ltd, Mumbai, India, sold the carbopol 934P. Every other chemical and reagent utilised was of analytical quality.

Compatibility study:

Pure drug, polymers and physical mixture of drug and polymers were subjected to differential scanning calorimetry (DSC) to study the compatibility between drug and polymers (DSC823E, Mettler Toledo system, aluminium pans were employed to place the samples. The heating rate was kept at 10º rise per min up to 200º to better integrate the information. Argon gas was used for purging.

Preparation of floating beads of famotidine:

Famotidine (20% w/w of dry polymer weight) was dissolved in water in acidic condition. SA (3% w/v) alone and polymer mixtures (3% w/v) containing SA and CP, and SA and HPMC K15 in 3 different ratios were dissolved in water to get clear polymeric dispersions, then a famotidine solution was added and mixed homogeneously. To the above mixture cod liver oil (20% w/w) was added and stirred to form a homogeneous emulsion. The drug-loaded emulsion was extruded through a 26-G syringe needle into calcium chloride solution (1% w/v) maintained under gentle agitation. The beads were allowed to remain in the same solution for 30 min to improve their mechanical strength. The formed beads were separated, washed with water and allowed to dry at room temperature overnight. Table 1 lists the formulation variables for different formulations of famotidine loaded floating beads. Blank beads without famotidine were also prepared using the same technique.

Evaluation of floating beads:

The prepared beads were evaluated for drug loading efficiency (LE) and drug entrapment efficiency (EE). An accurately weighed sample of beads (100 mg) was crushed in a mortar and added to 100 ml of phosphate buffer pH 7.4. This mixture was kept over night under stirring to elute complete drug from the polymer matrix. The mixture was filtered and analyzed spectrophotometrically at a wavelength of 265 nm (UV Spectrophotometer, 1601, Shimadzu, Japan) against blank bead mixture, which was treated similarly. The percent drug loading was calculated according to the following Eqn, percent LE = (drug load- drug loss)/drug load × 100 and the percent entrapment efficiency (%EE) was calculated according to the following Eqn, EE (%) = (actual drug content/ theoretical drug content)×100. The mean surface diameter of the beads was determined in dry state using a dial thickness meter.

TABLE 1: FORMULATION VARIABLES OF VARIOUS FAMOTIDINE BEAD FORMULATIONS

Formulation code	SA: CP (3% w/v)	SA: HK (3% w/v)	Oil (% w/w)
CF blank	10:0	10:0	20
CF1	9:1	-	20
CF2	8:2	-	20
CF3	7:3	-	20
CF4	-	9:1	20
CF5	-	8:2	20
CF6	-	7:3	20

SA, sodium alginate; CP, carbopol 934P; HK, hydroxypropylmethylcellulose K15; -, components not included in formulations.

Floating properties:

The time between the introduction of the FDDS into the medium and its buoyancy to the upper one third of the dissolution vessel (floating lag time) and the time for which the formulation constantly floated on the surface of the medium (floating duration) were measured simultaneously as a part of dissolution studies.

Swelling study:

The swelling behavior of the calcium alginate beads was studied in 0.1N HCl (pH 1.2) and phosphate buffer pH 7.4. Previously weighed (W1) beads were immersed in respective media. The weight (W2) of the beads was determined for 8 h: Every 30 min for the first 2 h and then every h after that. The swelling index (SI) of each batch was calculated using the following Eqn, percent SI = (W2 –W1)/W1 ×100.

In vitro drug release study:

In vitro release characteristics of famotidine floating gel beads were evaluated employing 0.1N HCl (pH 1.2). Dissolution of floating beads was carried out in a modified Rosette Rice test apparatus. A glass beaker of 100 ml was modified at the base by adding a tapped glass tube outlet so that the glass beaker can hold 70 ml of dissolution medium. This apparatus was housed inside an outer glass jacket through which hot water at 37±2º was circulated continuously. The medium was stirred at 75 rpm on a magnetic stirrer.

A burette connected to a reservoir was mounted above the beaker to deliver fresh dissolution medium at a flow rate of 10 ml/ 30 min. Sampling was done at every 30 min till 8 h. The

sample aliquots were analyzed spectrophotometrically at a wavelength of 265nm (UV Spectrophotometer, 1601, Shimadzu, Japan).

Stability study:

The formulation CF4 was subjected for three month stability study according to ICH guidelines by exposing the beads in a suitable packing mode to the temperature 40±2° and relative humidity 75±5% in programmable environmental test chamber (CHM-10S, Remi Instruments Ltd., Mumbai, India). At the end of every month the beads were analyzed for the drug content, floating behavior and in vitro drug release.

4. RESULTS AND DISCUSSION

Two endothermic peaks were seen in the DSC thermograph of pure famotidine (fig. 1a); the first was minor and located at 162.31°, while the second was sharp and located at 169.50°. The DSC thermograms of the physical combination of famotidine and the polymers revealed that the polymers lacked distinctive peaks, whereas the peaks of famotidine remained, albeit somewhat moved from their initial locations (fig. 1b to 1d). The results show that there is compatibility between the medication and the polymers.

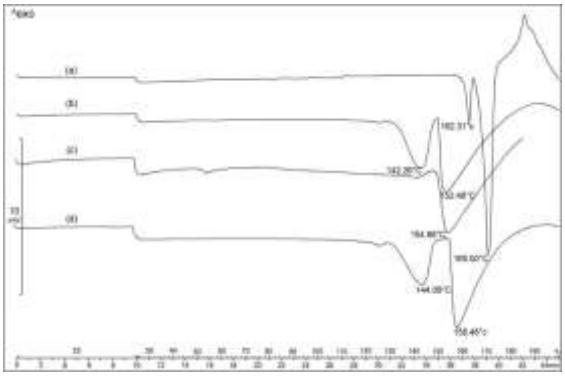


Fig. 1: Differential scanning calorimetry thermograms Differential scanning calorimetry thermograms of pure famotidine and with other polymers (a) FAM; (b) FAM/SA; (c) FAM/SA/CP 934P; (d) FAM/SA/HK 15M

Several famotidine bead formulations have drug loading percentages ranging from 39 to 53.5 (the active drug concentration varied between 0.848 and 1.561 mg in a 100 mg sample). Table 2 shows the entrapment efficiency for the different famotidine floating bead formulations, which ranged from 29.3 to 55.2%. The prepared beads were transparent and almost spherical. Table 2 provided the average surface diameter for each formulation. 1.734±0.006 (SD) to 1.751±0.032 mm (SD) is the range of the.

In addition to dissolving investigations, the produced beads' capacity to float was assessed. In 0.1N HCl (pH 1.2), the oil-free beads sunk right away, whereas the beads with 20% w/w cod liver oil (CF to CF6) showed instantaneous and superior floating ability. Table 2 shows the prepared beads' floating behaviour.

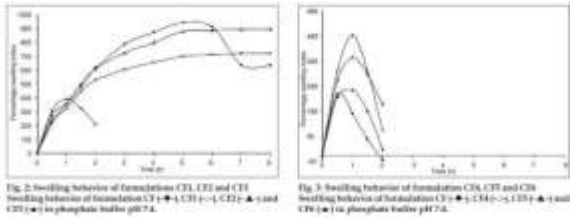
The beads' swelling behaviour was examined in 0.1N HCl and phosphate buffer (pH 7.4). There was no discernible change in the beads' swelling ratio in 0.1N HCl. The findings of the swelling indices of formulations CF to CF6 are displayed in figures. 2 and 3, and the beads exhibited notable swelling in phosphate buffer pH 7.4.

Famotidine floating beads were subjected to an 8-hour in vitro drug release investigation in 0.1N HCl (pH 1.2). The beads showed a biphasic release profile in the 0.1N HCl, with a burst effect (an initial quick drug release phase) followed by a sustained, steadily rising drug release phase that lasted for 1 hour and continued for up to 8 hours. Only SA in formulation CF was unable to maintain the famotidine release for eight hours. In contrast to formulations including CP, it released the whole drug after five hours and thirty minutes. At the end of eight hours, CF1, CF2, and CF3 released 50.94, 44.92, and 42.81% of the medication, respectively; the release profile is displayed in fig. 4.HPMC K15 was included in the formulations CF4, CF5, and CF6, which at the end of eight hours released 72.79, 67.70, and

65.57% of the medication, respectively. Figure 5 displays the release profile from these beads.

According to ICH criteria, a three-month stability study was conducted on formulation CF4 in light of the formulation's possible value. The formulation was put through in vitro release investigations, floating behaviour tests, and drug assays at the end of each month. Table 3 and Figure 6 presented the findings.

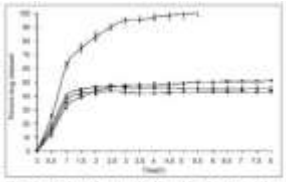
TABLE 1: EVALUATION PARAMETERS OF VARIOUS FAMOTIDINE BEAD FORMULATIONS



No potential drug-polymer incompatibility was shown by the thermograms produced by applying both pure famotidine and a physical combination of famotidine and polymers (fig. 1). In contrast to the famotidine peaks found in the physical mixtures of famotidine and polymers, which were broader and slightly shifted from their original positions, the thermograph of pure famotidine displayed a sharp peak at 169.50°. This could be because of the presence of other functional groups of polymers that may be overlooked.

Ionotropic gelation of alginate with divalent calcium ions can result in gel formation. Intermolecular cross-links between the negatively charged alginate molecules and the divalent calcium ions were created when an emulsion of cod liver oil containing alginate was placed into calcium chloride solutions, resulting in the rapid formation of spherical beads. Without the need for complex equipment, the gel beads were simply manufactured. The emulsion must be homogenised since, even when stirred, the oil would separate from the alginate solution without homogenisation. During the homogenisation process, alginate may have contributed to the emulsification of the water and oil phase combination. However, when the oil content was raised to over 30%, the emulsifying ability was restricted. The oil began to seep out of the beads at this concentration and higher. The round, transparent, and faintly yellowish beads were caught in oil. It was discovered that in order to provide the beads adequate buoyancy, at least 20% w/w cod liver oil was required.

Table 2 displays the famotidine-loaded beads' percentage drug loading efficiency (%LE). The percentage LE was found to be between 39% and 53%. The formulation CF provided the lowest %LE, whereas CF 5 provided the greatest %LE. In a similar vein, Table 2's percentage entrapment efficiency for the beads fell between 29% and 55%. The formulations with the highest and lowest drug entrapment, respectively, were CF2 and CF. Because the alginate matrix is so porous, the drug may leak back into the cross linking solution from the bead matrix during the cross linking time, which might account for the low drug loading and low entrapment effectiveness of the CF formulation. Higher viscosity copolymers like CP and HPMC K15 may have been added to the polymer matrix, increasing its viscosity and creating a stiff barrier that prevented the medication from diffusing back into the cross-linking solution. In comparison to CF formulations, formulations containing these copolymers demonstrated superior drug loading and drug entrapment efficiency. The results further demonstrate how copolymers promote drug loading in the beads, with higher copolymer concentrations in the bead formulation further improving drug loading and drug entrapment efficiency.



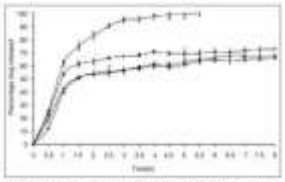


TABLE 3: STABILITY STUDIES OF FORMULATION CF4

Formulation code	Drug content ±SD (mg)	Floating behavior		Drug release at the end of 8h
		FLT (min)	Floating duration	
Zero month	0.966±0.035	0	24	72.79±0.310
First month	0.971±0.158	0	24	71.54±0.321
Second month	0.963±0.340	0	24	70.92±0.297
Third month	0.970±0.155	0	24	71.04±0.685

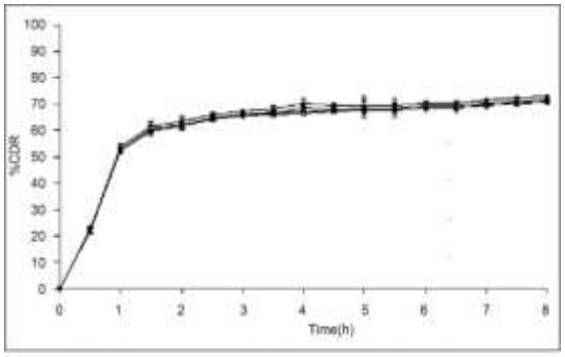


Fig. 6: ***In vitro*** **drug release profile of CF 4 during stability study** ***In vitro*** **drug release profile of CF 4 after zero (-◆-), first (-□-), second (-▲-) and third (-■-) month of stability study.**

The drug loading to the beads causes the size of the formulation CF beads to grow to 1.751±0.032 (SD) mm, whereas the mean particle diameter of the blank oil-entrapped alginate beads without drug was determined to be 1.714±0.052 (SD) mm. As with formulations CF1 through CF6, the bead diameter decreases when copolymers are added to the bead formulation. The additional ingredients caused the calcium alginate beads' size to vary, even though the procedure settings remained same. In addition to dissolving investigations, the produced beads' capacity to float was assessed. In 0.1N HCl (pH 1.2), the oil-free beads sunk right away, whereas the beads with enough cod liver oil (CF to CF6) showed outstanding and instantaneous floating ability. The beads stayed afloat for the whole eight-hour research session and for the full twenty-four hours. Therefore, it was discovered that the amount of oil contained in the polymer matrix was closely correlated with floating ability.

The bead's swelling behaviour was investigated in 0.1 N HCl and phosphate buffer pH 7.4. The beads' swelling ratio in 0.1 N HCl was Figure 6: CF 4's in vitro drug release profile during a stability investigation CF 4's in vitro drug release profile following a stability analysis of zero (-⊓-), first (-□-), second (-▲-), and third (-■-) months. Not much changed. Additionally, there was no discernible swelling or erosion of the beads in the 0.1N HCl dissolving medium. Based on these findings, it may be inferred that the drug release was governed by the famotidine's dissolution in the dissolution liquid and its diffusion through the polymer matrix, rather than the swelling behaviour. On the other hand, beads inflated and degraded in the interim when exposed to phosphate buffer pH 7.4. CF formulation, Within the first hour of the research, it swelled to its maximum, but by two hours, it had totally eroded. Formulations including CP, such as CF1 and CF2, exhibited swelling that increased until 8 hours, whereas CF3 had the greatest swelling at the end of 5 hours. Following this, the bead matrix began to erode (fig. 2). After one hour, all of the formulations containing HPMC K15—CF4, CF5, and CF6—swelled to their maximum size, and after three hours, they were totally corroded. After one hour, the gel beads in the 0.1 N HCl (pH 1.2) showed a slower, prolonged, and steadily rising drug release phase, which was followed by an initial fast drug release phase. Within one hour, Formulation CF released 62.37±2.21% of the medication; however, it was unable to maintain this release over the next seven hours, and at the end of five hours and thirty minutes, 100% of the drug was released. The medication was released in 50.94, 44.92, and 42.81% of formulations CF1, CF2, and CF3 that contained CP and SA after 8 hours (fig. 4), and in 72.79, 67.70, and 65.57% of formulations CF4, CF5, and CF6 that contained HPMC K15 after 8 hours (fig. 5). The findings demonstrate

that the medication release from the oil-entrapped calcium alginate beads may be sustained by the addition of rate-controlling polymers such CP and HPMC K15. The results further demonstrate that the drug release was further reduced and more sustained when the concentration of both copolymers in the formulation increased.

To clarify the process of drug release from the floating gel beads, a variety of release kinetic models, including zero order, first order, and Higuchi and Korsemeyer Peppas models, were applied to the data gathered from in vitro release investigations. Table 4. Fitting the formulation CF to the first order equation revealed a higher r2 (r2 = 0.9892), suggesting a first order release from the formulation CF. In contrast, the Higuchi model was followed by all other formulations, CF1 through CF6. The drug release from the beads was thought to follow fickian diffusion as the n values of the Korsemeyer-Peppas model for all formulations were found to be less than 0.5. The formulation CF4's stability investigation revealed no appreciable changes in the drug content, floating behaviour, or in vitro drug release properties of the bead formulations.

TABLE 4: KINETICS OF IN VITRO FAMOTIDINE RELEASE FROM FLOATING BEADS

Formulation code	Zero order (r^2)	First order (r^2)	Higuchi model (r^2)	Korsemeyer model (n)
CF	0.713	0.9892	0.9525	0.4936
CF1	0.566	0.6331	0.7974	0.3606
CF2	0.2129	0.3188	0.5622	0.1943
CF3	0.3618	0.3796	0.6088	0.2275
CF4	0.5011	0.6237	0.7424	0.2956
CF5	0.6489	0.7821	0.8501	0.4538
CF6	0.6005	0.7228	0.8242	0.3402

5. CONCLUSION

Floating drug delivery systems (FDDS) represent a significant advancement in the formulation of controlled-release drugs, particularly for drugs like chlorthiazide, which suffer from limitations such as poor bioavailability and short half-life. The development of floating tablets for chlorthiazide can enhance its therapeutic efficacy by extending its gastric retention time and providing sustained drug release, thus reducing the dosing frequency and improving patient compliance.

The use of excipients like hydroxypropyl methylcellulose (HPMC) and effervescent agents such as sodium bicarbonate has shown positive results in maintaining buoyancy and achieving controlled drug release. Optimization techniques like response surface methodology (RSM) have proven effective in fine-tuning formulation parameters to improve drug release profiles and stability.

While the preclinical results are promising, challenges such as variability in gastric conditions and stability during storage still need to be addressed. Future research should focus on refining the formulation, conducting clinical trials, and exploring new excipients to enhance the performance and clinical applicability of floating drug delivery systems.

In conclusion, FDDS formulations of chlorthiazide offer a promising strategy for improving its pharmacokinetic profile and can be extended to other drugs with similar challenges, ultimately benefiting both patients and healthcare systems.

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