Available online on 15.08.2024 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Review Article

An Updated Overview of Gastro-retentive Floating Drug Delivery Systems: Formulation Strategies and Application

Surender Kumar [1], Jagtar Singh Chohan [1], Harwinder Kaur [1], Rishabh Kasnia [1], Sunaina Demiwal [1], Bhupender Nehra [2]*

[1] *Department of Pharmaceutical Sciences, Lord Shiva College of Pharmacy, Sirsa-125055, Haryana, India*

[2] *Department of Pharmaceutical Sciences, Guru Jambheshwar University of Science & Technology, Hisar-125001, Haryana, India*

Article Info:

Article History:

Received 17 May 2024
Reviewed 02 July 2024
Accepted 28 July 2024
Published 15 August 2024

Cite this article as:

Kumar S, Chohan JS, Kaur H, Kasnia R, Demiwal S, Nehra B, An Updated Overview of Gastro-retentive Floating Drug Delivery Systems: Formulation Strategies and Application, Journal of Drug Delivery and Therapeutics. 2024; 14(8):175-182

DOI: http://dx.doi.org/10.22270/jddt.v14i8.6726

*Address for Correspondence:

Mr. Bhupender Nehra, PhD Research Scholar, Department of Pharmaceutical Sciences, Guru Jambheshwar University of Science & Technology, Hisar-125001, Haryana, India;

Abstract

Gastro-retentive floating drug delivery systems (GRFDDS) have emerged as a significant advancement in enhancing the bioavailability and therapeutic efficacy of various medications. This review article provides a comprehensive overview of recent innovations in GRFDDS, highlighting their formulation strategies, mechanisms of buoyancy, and various applications in drug delivery. The role of various polymeric materials, gas-forming agents, and optimization techniques is discussed which are generally employed to develop effective floating systems. Additionally, keen insight is brought on applications of GRFDDS in treating gastrointestinal disorders, enhancing the pharmacokinetics of drugs with narrow absorption windows, and their potential in controlled-release formulations. In this review, authors compiled the recent reported literatures about the gastro-retentive floating drug delivery systems since 2015 to underline the effectiveness and safety profiles of these systems. This review aims to consolidate current knowledge and inspire future research directions in the development of GRFDDS for improved patient outcomes.

Keywords: Floating; Gastro-retentive; drug delivery; HPMC; Effervescent

Introduction

From last few decades, Human beings have always suffered from illnesses and diseases in one way or another. They have developed many dosage formulations that can be administered through various methods. However, oral route has gained popularity for drug administration due to a large number of advantages associated with it. The major objectives of any drug delivery method are to afford a healing dose of medication at the required body part in quick and sustained manner. Now a days, different dosage formulations have been invented with diverse range of routes administration.[1] Among those all, oral drug delivery system is considered as most exploited drug administration route by the researchers. Oral medication delivery methods make up approximately more than half of drug delivery approaches present on the market.[2] The most widely employed route for systemic drug administration among all the ones that have been studied in different medicines is via oral ingestion. Because oral dosage forms are inexpensive, easy to administer, and have flexible handling and formulation, patient compliance is very high while using them.[2,3] Some significant aspects that affect oral medication delivery effectiveness include the speed at which dosage forms pass through the gastrointestinal tract, the location of drug absorption, and the gastric emptying process. The majority of oral dosage forms have a variety of physiological limitations, including variable gastrointestinal transit. This is due to variable gastric emptying, which causes an uneven absorption profile, insufficient medication release, and a lesser dosage form retention time in the stomach.[4] As a result, medications have an insufficient absorption window and remain unabsorbed, particularly in the top section of the small intestine. Thus, gastric emptying time is completely dependent on several factors that are present in both within and between subjects.[5] The gastrointestinal tract imposes many different obstacles that conventional technologies are unable to overcome. Therefore, the true difficulty in creating a controlled drug delivery approach was not only to maintain drug proclamation but also to extend the formulation's residence period in upper small intestine or stomach until entire drug was released at the required pace.[6]

Gastro Retentive Drug Delivery Systems

Gastro Retentive Drug Release Systems can improve the controlled release of drugs with an absorption window by continuously releasing the drug for a prolonged amount of time before it reaches its absorption site. Table 1 illustrates the primary distinctions between the gastro-retentive drug delivery system (Figure 1) and the standard drug administration method.

Table 1: Conventional DDS v/s gastro-retentive DDS[7]

Sr. No.	Factors	Conventional DDS	GRDDS
1.	Adverse effect	Chances of side-effect is high	The risk is low
2.	Attentiveness of patients	The rate is very low	It improves patient compliance
3.	Dose overflowing	More chances of dose dumping	At no danger
4.	Drugs with narrow absorption window	Not much useful	It is advantageous
5.	Drugs with localized effect in stomach	Lesser useful	It is beneficial
6.	Drugs with poor solubility in alkaline pH	Not much useful	It is advantageous
7.	Drug which degrades in the colon	Not much advantageous	Very much advantageous

GRDDS is an effective approach consist of a medication which can be administered orally and stay in abdomen for some hours, extending the duration of its gastric residential time. GRDDS improves effects of medications that act in the stomach, with a limited absorption in upper GI tract, or have poor stability in the colon. GRDDS can thereby enhance both compliance and the bioavailability of the medications.[7]

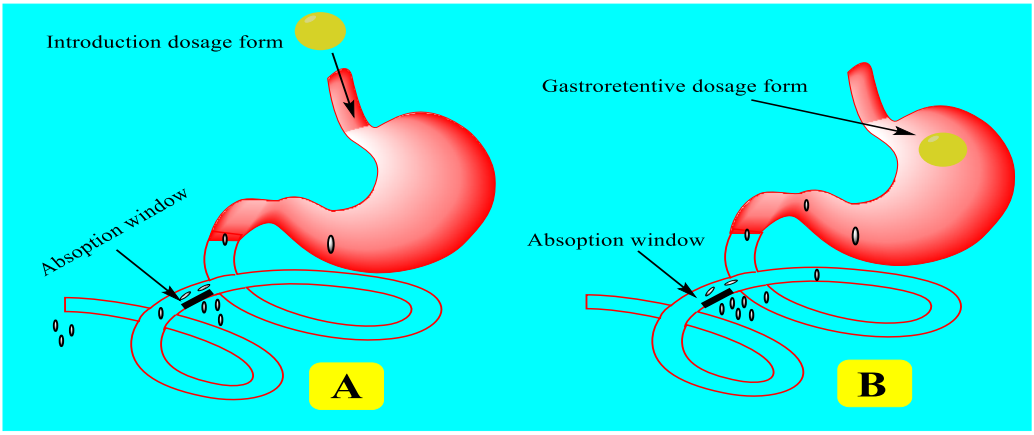

Figure 1. Conventional v/s Gastro retentive drug delivery system

Higher gastric retention is beneficial for drug release to stomach as well as small intestine, as well as for enhancing bioavailability, reducing drug waste, and enhancing solubility in a high pH environment.[7,8] Many physiological restrictions can be lessened or eliminated by gastro-retentive systems, improving a drug's therapeutic efficacy.

Different strategies pursued since the last several years, to enhance the gastric residency period of oral dosage forms in abdomen. There are several techniques to developing prolong gastric retention (Figure 2) have been investigated.

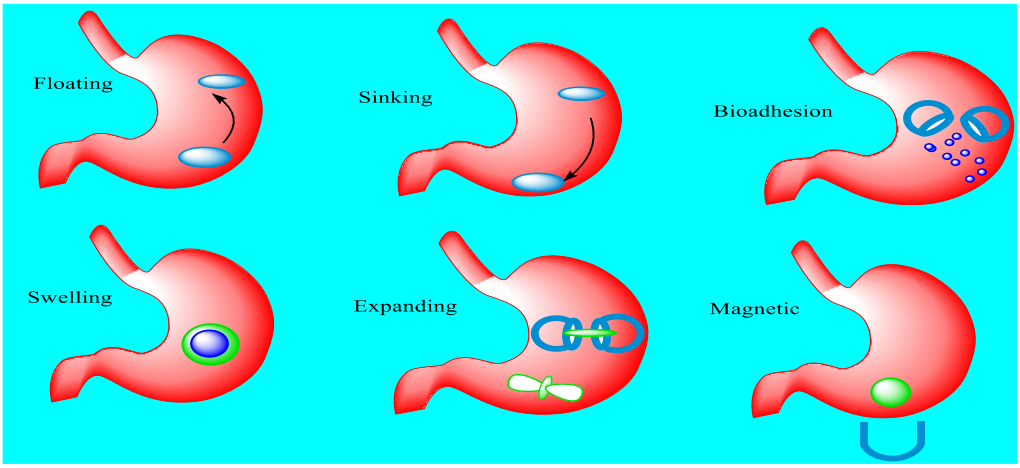

Figure 2. Approaches to gastro retentive drug delivery system

Floating Drug Delivery System

One important tactic for attaining stomach preservation and sufficient drug bioavailability is the use of floating drug delivery systems. This mode of administration is recommended for drugs that have an absorption in the gut or upper small intestine. Because these systems have less bulk density as compared with gastric fluids, they can float in the stomach for a longer duration without looking for gastric emptying rate.[9-11] Floating drug delivery systems, or hydro-dynamically balanced systems, are modest density items that drift in stomach for a prolonged period of time lacking impeded the stomach's emptying process. Their density is lower than that of gastric fluid. Longer stomach retention and improved management of such variations in plasma medication concentrations are the outcomes of this. Numerous buoyant systems have been created, including those based on laminated films, hollow microspheres, tablets, capsules, powders, and granules.[12,13] Floating systems might be based on effervescence or on an intrinsically low density. The intrinsic low density of non-effervescent systems can be attributed to swelling, the inclusion of low-density material (sponges), lower dense hollow microspheres trapping air, or both. On the other hand, effervescent systems have a high initial bulkiness that reduces when they come into touch with an acidic environment because CO_2 is formed.[14,15]

Classification of Floating Drug Delivery system

Floating medication delivery approaches are generally of two kinds which includes effervescent and non-effervescent techniques. The effervescent system uses matrices produced with chitosan, effervescent substances which hold a liquid that, when heated to body temperature, may transform into a gas. It is reported that even a stoichiometric ratio of 0.76:1 is optimum for gas generation when using citric acid and sodium bicarbonate. These approaches are usually developed with the help of ethyl cellulose coated and carbonate loaded resins.[16] Water can permeate via in better proportion through a permeable coating material. Because of the CO_2 released, the resin drift in gut as a result. The gas generated system (floating pills, floating system with ion exchange resin), the inflatable GI delivery method, and the intragastric osmotically regulated drug delivery method are further subcategories for effervescent system. On the other hand, in non-effervescent systems, swallowing index, system types, and formulations all play a major role in how long the particles stay in the gastric fluid and how difficult it is for them to pass through the stomach. Alginate beads, Hydro dynamically balanced system (HBS), Hollow microspheres, and Micro-porous compartment system are further subclassifications of the non-effervescent system.[17,18]

Literature review focused on gastro retentive floating drug delivery systems

Katekar *et al.,* (2023) discussed a review on recent advantages and evaluation of microparticles and their applications. Microparticles, composed of synthetic, non-biodegradable polymers ranging from 1 to 1000 microns, offer two main types: microcapsules and micro matrix. These include magnetic, polymer, bio-adhesive, biodegradable polymer, synthetic polymer, floating and radioactive microparticles. Unlike nanoparticles, microparticles remain localized within the 100 nm interstitium during lymphatic transport. The transcript also introduces methods for characterizing various physicochemical parameters, such as drug release, thermal properties, and particle size, along with innovative tests like *in vitro* leaching and floating tests.[19]

A review of the features and facts of gastro-retentive floating medication delivery systems was published by Mahalakshmi *et al* in 2023. Floating Drug Delivery Systems (FDDS) have a unique approach that includes the creation of single and multi-unit floating systems, the incorporation of newly discovered polymers, and the management of formulation and physiological variables that impact stomach retention. It involves methods for combining gas-generating substances with tablets or capsules to create floating dosage forms. The review also looks at current, cutting-edge advancements in the industry.[20]

The goal of Kothule *et al*.'s analysis of internal drug delivery method in 2023 was to summarize the research findings by emphasizing cutting-edge intestinal methods that have become the standard in the field of oral controlled medication delivery. In order to understand the physiological difficulties involved in attaining stomach retention, we compiled the key variables affecting it. Numerous intestinal techniques were investigated, including those that were floating, biological or mucosal, inflatable, brittle, ultra porous, high-density (sink), and magnetic. In the end, a full discussion of the many advantages of medication delivery systems in the gastrointestinal tract took place.[21]

An overview of gastro-retentive drug delivery methods is presented by Tafisha *et al* (2023). To improve bioavailability, Gastro-retentive drug delivery method was formed for prolonging drug's gastric retention time. GRDDS prove valuable in treating gastrointestinal illnesses offering site-specific drug administration and improving absorption of stomach-soluble drugs. The discussion encompasses various GRDDS techniques, including floating and non-floating systems, each with sub-types. The review also includes recent patents on GRDDS and a comprehensive description of assessment parameters.[22]

Mangifera indica gum was developed and evaluated as a sustained release polymer in glibenclamide matrix tablets, according to Dwivedi *et al* (2023). Because they have a lower bulkiness than stomach fluids and floating drug delivery approach, can float in the stomach up to longer duration without slowing down the rate at which the stomach empties. The current study used the solvent evaporation method to formulate and assess a floating tablet of the highly water-soluble anti-diabetic medication glibenclamide (GL), with Mangifera indica gum serving as the polymer.[23]

The manufacture and assessment of gastro-retentive floating matrix tablets containing bilastine were demonstrated by Ranjeeth *et al* in 2023. This work explores bilastine formulations that are gastro-retentive by utilising a variety of polymers and sodium bicarbonate as an effervescent agent. Bilastine effervescent floating matrix pills were created by methodically investigating natural and manmade polymers either separately or in combination. With a zero-order profile and a lag time of less than two minutes, the optimized formulation containing HPMC floated for twelve hours and showed extended *in vitro* drug delivery. The nature of the gel matrix is related to the release process, emphasizing the importance of polymer swelling. In order to achieve buoyancy, prolong the period that a drug is in the stomach, and maybe increase drug bioavailability, effervescent-based floating drug delivery shows promise.[24]

Lamivudine extended-release floating tablets was formulated and evaluated via employing xanthan gum and HPMC polymers were revealed by Wathore *et al* in 2023. The goal of this project was to create floating tablets, or other gastro-retentive devices, that would release lamivudine gradually over a number of hours. The formulations (F1-F9) were subjected to comprehensive evaluation, which included a study of drug-polymer compatibility. They were made using rate-modifying polymers like xanthan gum, HPMC K100M and HPMC K15M.

The fabrication process was successful, according to the pre- and post-compression evaluations.[25]

In their discussion of the formulation and assessment of floating pantoprazole sodium tablets for peptic ulcers, Rajput and their group (2022) demonstrated the use of floating drug delivery methods to increase drug's flexibility over gastrointestinal fluids and, as a result, sustain its prolonged duration of action. The results showed that the drug content ranging from 97.11 to 99.56, the floating duration was greater than 12 hours while floating lag time was not more than 60 seconds. For every formulation, *in vitro* drug release findings ranged from 82.27 to 97.6 in a 12-hour period. It was shown that pantoprazole floating decreased the frequency of doses and lengthened the medication's half-life in the stomach.[26]

Gangwar *et al*.'s (2022) creation and assessment of a biodegradable floating drug delivery system for improving diclofenac sodium solubility was shown. The goal of the research is to evaluate how pharmacological limitations affect the characteristics for gastric floating tablets by using diclofenac sodium (standard) for improving solubility. To improve solubility, calcium carbonate ($CaCO_3$) or sodium bicarbonate ($NaHCO_3$) are used. For the purpose of creating floating DICL tablets, swelling polymer like HPMC in association of K15M or K100M. Direct-compression manufacturing was employed in this process. Through the use of DSC and FTIR, *in vitro* proclamation under non-reducing circumstances was assessed.[27]

Mehetre *et al*., (2022) talked about the development and assessment of a ciprofloxacin hydrochloride-containing hydrodynamically balanced gastro-retentive drug delivery method. The floating tablets were evaluated for a 12-hour in-vitro release after being directly compressed with the help of HPMC K4M as well as K15M polymers with some effervescent agents like $NaHCO_3$. It was found that one important element affecting buoyancy was tablet hardness. For more than 12 hours, all formulations demonstrated acceptable floating qualities. The formulation comprising 200 mg HPMC K15M (F4) showed sustained release in *in vitro* release experiments, indicating a potential strategy for controlled release and enhanced bioavailability in comparison to previous batches.[28]

Flurbiprofen floating matrix tablet formulation and evaluation were documented by Kalita and their co-workers in 2021. created a floating drug delivery method that increases bioavailability and therapeutic efficacy of flurbiprofen by utilizing several polymers like PEO and HPMC K100M. Sodium bicarbonate was added as an agent that produced gas. In the study that was given, the direct compression method was employed. In order to achieve acceptable tablet qualities such as uniform thickness, consistent weight homogeneity, friability, and optimal hardness, the formulation was optimized. Under the tested parameter, the prepared formulation yielded more favorable and noteworthy outcomes.[29]

Bakre *et al*., (2021) reported on the formulation and assessment of Ibuprofen Matrix tablets with sustained release, utilizing maize genotype starch as the polymer. The polymer-drug composition as well as kind of polymers were varied using a 32-factorial design, while the times needed for 50% (T50) and 90% (T90) drug release were varied as dependent variables. Super case transport was shown to be the main release mechanism, and drug release followed the Higuchi model. Various kind of polymer interacted to considerably extend cumulative drug release and dissolution timeframes (T50 and T90). It is possible to quantitatively alter the drug release characteristics of maize starch in pharmaceutical formulations by modifying its genetic makeup, as evidenced by the improved sustained release of starches from genetically changed cultivars through erosion and polymer relaxing.[30]

The development and evaluation of a bilayer tablet for the successful treatment of stomach ulcers was revealed by Singh and his team in 2021. pylori-induced stomach ulcers to lessen the frequency of medication administration and lessen adverse effects. The tablets had a round shape, were white, and were determined to be uniform in context of hardness, alteration in mass, friability as well as content uniformity across batches. The medicine was distributed uniformly throughout all formulations. After 12 hours, the GRF tablets' in-vitro drug proclamation revealed within a 98.15% range.[31]

The distribution of formulated free-floating matrix tablets was assessed and evaluated in anti-parkinsonism was reported by Lokeswara *et al* (2020). utilizing a variety of excipients and an effervescent system, the sustained-release floating tablets were created utilizing the direct compression strategy. Rate-retarding polymers such as Carbopol and Hydroxypropyl Methyl Cellulose (HPMC) were also included. The tablet's performance was assessed in 0.1N HCl at ideal temperature, taking into account the *in vitro* drug release, floating lag time, and floating time. Tablets comprising 40 mg HPMC K15 M and 110 mg HPMC K100 M (F9) shown good drug release over a 24-hour period. In contrast, tablets containing 100 mg and 50 mg of HPMC K100 M K15 M, respectively (F8), which did not contain microcrystalline cellulose (MCC), demonstrated favorable release characteristics. Polymer suitability was established by compatibility investigations using FTIR and DSC. Ninety days of accelerated stability testing revealed no discernible alterations in drug release. Using HPMC K100 M and HPMC K15 M, the matrix-type floating drug delivery system efficiently extended the stomach residence duration and sustained the release of more polar medication pramipexole.[32]

The formulation as well as *in vitro* evaluation of metformin sustained release matrix tablets made with detarium microcarpum gum were covered by Okafo *et al* in 2020. Acetone desolvation was used to extract Detarium microcarpum gum (DMG) from macerated powdered seeds. Metformin matrix pills were thoroughly tested, either in conjunction with sodium carboxymethylcellulose (NaCMC) or DMG alone. The tablets' appropriate hardness, friability, and drug content were accompanied by desired physical qualities that were similar to those of a commercial product. MTF2 and MTF6 formulations with 30% and 20% of DMG, respectively revealed remarkable prolonged release, releasing 75% in 7-9 hours and the whole amount in more than 12 hours. DMG has been successfully used in the manufacture of metformin matrix tablets, either by itself or in conjunction with NaCMC. long-term delivery of metformin matrix pills that were equivalent of formulation that was sold.[33]

Using melt extrusion technology, Vo *et al* (2020) detail the constant trade of ketoprofen sustained release pellets through the use of inline pellet size analysis, inline near infrared, and QbD design space. The study presented a novel method for continuously producing delayed-release dose forms utilizing hot-melt extrusion. Drug release parameters were associated with input factors using a full factorial design. This association was effectively highlighted by the PLS fit approach. After 120 minutes, the three variables affected the drug's release in the simulated gastric fluid, but the stearic acid content had no discernible effect on the drug's solubility in the simulated intestinal fluid. Multiple contours from regression equations were used to identify an optimized formulation and design space. Particle size analysis and inline NIR were used to successfully monitor continuous manufacturing, ensuring that the medication load and pellet size were under control. In stomach fluid, the resulting pellets showed less than 5% release after 120 minutes, but in intestinal fluid, they showed approximately 85% and 95% release after 30 and 45 minutes, respectively.[34]

In their formulation and evaluation of floating matrix tablets, Bhambar and their group (2019) looked at the prolonged release of Drotaverine Hydrochloride, an efficient muscle relaxant for managing spasticity. Roughly 95% of the hydrochloride rotaverine binds to plasma proteins and is metabolized in the liver. The tablets were designed with a gastro-retentive dosage for targeted medication release in the stomach. They were created by direct compression using effervescent agents. To slow down medication release, ethyl cellulose and HPMC K100M were utilized. The polymer proportion in the tablets was shown to be adequate to prolong drug release for a minimum of 12 hours, according to evaluation. At the 12-hour period, FT-6 demonstrated the highest drug release (79.37%) among the formulations, while FT-7 showed the lowest (46.33%).[35]

In 2019, Eziuzo and colleagues created floating matrix pills containing ciprofloxacin, utilizing polar polymer like sida acuta gum or SAG. SAG was separated from dried, powdered sida acuta leaves and used directly into tablet formulation. The tablets containing 20% hydroxypropyl methylcellulose (CF4) showed about 5000% swelling. The SAG, HPMC and SCMC polymer percentages for CF1 (110% drug release), CF2 (72% drug release), CF3 (106% drug release), CF4 (46% drug release) and CF5 (87% drug release) were 20% (SAG), 30% (SAG), 30% (SAG and HPMC), 20% (HPMC) and 20% (SCMC) after 7 hours, respectively. The study found that sida acuta gum worked well like hydrophilic polymer to create controlled release ciprofloxacin floating matrix tablets.[36]

Devi *et al*., (2019) provided an effervescent technology-based demonstration of the formulation and assessment of gastro-retentive floating Diclofenac sodium tablets. The effervescent technology of the dry granulation method was utilized throughout formulation of the tablets, with effervescent ingredient ($NaHCO_3$). Citric acid and sodium bicarbonate were used to provide buoyancy, while HPMC and MCC were employed as a hydrophilic swellable polymer and to regulate medication release. Five formulations containing different amounts of MCC and HPMC were made. F5, disclosed the floating lag time (40 seconds) with medication release of 33.17% in 12 hours. Further, *in vitro* dissolution characteristics suggested that drug delivery could be prolonged by increasing the amount of polymer. The investigation came to the conclusion that HPMC and effervescent agents may be incorporated for creating gastro-retentive floating tablets that would guarantee steady and comprehensive medication release over a prolonged amount of time.[37]

In their 2018 study, Nagori *et al*., talked about how to make and assess ketoprofen sustained release matrix tablets using natural gums. Wet granulation was used to formulate ketoprofen's prolonged release matrix tablets. Talc was employed as a lubricant and gum damar as a hydrophilic release retarding polymer. studies on *in vitro* dissolution and model fitting evaluation. The produced tablets' *in vitro* emissions of ketoprofen were observed in pH 1.2 buffer and pH 6.8 buffer for 2 and 6 hours, respectively. The formulation batch F3 exhibited an approximate 85% drug release rate; this could be attributed to either a high drug-to-polymer ratio or a significant gum damar swelling that retards the drug release. The formulation that was created yielded improved and noteworthy outcomes for every parameter that was undertested.[38]

The preparation and assessment of ketoprofen's sustained-release formulation regarding extended drug release was done by Zhang and their colleagues (2018). The chitosan and poly (lactic-co-glycolic acid) implants were used to formulate the tablet. There were no surface flaws or fractures, and the implants seemed uniformly rounded and smooth. The drug content varied from 89.98 ± 2.06 to 92.95 ± 1.65%, with friability less than 1%. After five days, the *in vitro* drug release was demonstrated in the range of 70-92%. The implants with the largest edoema (40.24 ± 1.08%) were those with a larger PLGA concentration. In the hot plate procedure, inserted IKT3 revealed highest analgesic potential and shortest duration i.e., less than 3 hours of extreme analgesia. After 24 hours, the percentages of IKT1, IKT2, and IKT3 that inhibited rat paw edoema were 79.95%, 69.98%, and 82.24%, respectively. Finally, the analgesic effect of ketoprofen-loaded IKT3 had a comparatively rapid onset and a lengthy half-life.[39]

In their 2018 paper, Dumpa *et al*., present a novel method for creating a continuous hot-melt extrusion (HME) Chronotherapeutic Drug Delivery System (CTDDS). Ketoprofen and ibuprofen are employed as core pharmaceuticals while using Eudragit S100 and ethyl cellulose for formulation of matrix and release retardation purpose, respectively. EC content and particle size were significantly proven as dependent variables in case of drug release. For instance, KTP release was maintained for 22 hours by 5% EC pellets. A six-hour lag period was found to be desirable in *in vitro* experiments using three-stage dissolving media.[40]

Raza *et al*., (2017) developed, assessed, and improved floating tablets containing minocycline hydrochloride. Carbopol 934, Methocel K15M and Methocel K100LV were chosen as the polymers to be used in the direct compression method of making the floating tablets. It was observed that Carbopol 934 significantly enhanced the release rate of drug while Methocel K100LV and K15M depleted the drug release rate.[41]

It was concluded that floating time were decreased via the use of Carbopol 934 in formulations while encouraged at significant level through incorporation of Methocel K15M and K100LV. The formulation of floating Bio-adhesive compression coated micro pills of Valsartan was done by Vemula *et al* (2017). Using a wet granulation technique, polymers like HPMC KAM and Carbopol 934P were used to crush coat the core mini-tablets. Based on the findings, formulations with a 1:1 ratio of HPMC KAM to Carbopol 934P demonstrated regulated release as opposed to the other ratios of both polymers. A floating time of more than 12 hours was demonstrated by the optimal formulation, which contained both polymers in a 1:1 ratio. and there was a controlled distribution of the drug.[42]

In this case, gastro-retentive floating matrix of stavudine was developed, optimized, and *in vitro* characterized by Rupavath and their team (2016). Pullalun gum and HPMC K15M were used as polymers in the wet granulation process that was used to create the tablets. The formulation including HPMC K15M was found to exhibit regulated release for up to 16 hours, and it was also noted that the buoyant duration exceeded 16 hours. Compared to the formulation including gum, the formulation incorporating HPMC K15M was shown to have a longer floating lag time.[43]

Gastro-bilayer floating tablets containing Atenolol and Simvastatin as sustained release layer and immediate layer, respectively were developed and assessed by Swain *et al* (2016). Using effervescent agent like $NaHCO_3$ and hydroxypropyl methylcellulose K100 (37.5%) for retarding the release rate, gastro-bilayer floating tablets were optimized using direct compression technique. The sodium starch glycolate super disintegrant polymer made up the instant release layer. The pills with the optimal formulation were seen to float on the test medium for almost 12 hours, with a 9-minute floating duration. It was determined that the formulation of gastro-floating bilayer tablets in this investigation was successful in achieving the biphasic drug release pattern, which was prolonged for 12 hours through diffusion process and more than 96% release of simvastatin in less than half an hour.[44]

Hibiscus rosa-sinensis leaf mucilage was incorporated to formulate the ketoprofen sustained release matrix tablet followed by its evaluation, as reported by Kaleemullah and their group (2016). This work was dedicated to prepare Ketoprofen matrix tablets with the mucilage of Hibiscus rosa-sinensis leaves and HPMC (K100M) by direct compression to achieve sustained drug release. 78.03% is the best formulation's F2 value. No discernible variation ($p > 0.05$) was found in the statistical analysis between F3 and the reference medication, suggesting that F3 is a viable formulation to be further explored in sustained-release matrix tablets.[45]

Ammar and their co-workers (2016) used the solvent diffusion approach to create floating microparticles of risperidone. *In vitro* experimental performance of the optimized floating microparticles was good, with a floating ability of up to 95.93% for a 12-hour period. *In vivo* x-ray investigations were also used to validate this floating ability. Pharmacokinetic studies demonstrated that the optimized formula had significant p value less than 0.05 with elevated AUC and t_{max} values and lesser C_{max} value when compared to marketed oral product. These findings suggest that the optimized formula has gradually released properties, which contribute to the drug's high treatment efficacy and decreased extrapyramidal side effects.[46]

By integrating the floating and swelling mechanisms, Bera *et al*., (2016) observed the HPMC-based gastro retentive dual functioning matrices covered with calcium ions got tethered in cross linkage with alginate-fenugreek gum gel membrane for intragastric quetiapine fumarate. Citric acid concentrations and polymer blend proportions were found to have an impact on medication release. The formulation's optimized tablets, HPMC K4M: HPMC E15, with an 80:20 polymer ratio, showed a t50% of 247.67±3.51 minutes and a drug release of 71.11±032% after 8 hours. The optimized matrices covered with biopolymers demonstrated enhanced buoyancy, favored swelling properties, and a reduced rate of drug release.[47]

Kesarla and their colleagues (2015) developed and assessed the absorption of a floating tablet containing the H2-receptor antagonist ranitidine hydrochloric acid by employing the sublimation method. Then, using polymer as well as sublimating material, a 32 factorial design was used. A few excipients like L-menthol, POLYOX WSR N 60 K and Klucel-LF were used in the sublimation process to make matrix tablets. A systematic design was chosen to investigate ideal concentration of 40 mg L-menthol and 420 mg POLYOX to achieve 90% drug release in 12 hours. Formulation stability was confirmed by stability studies. The resulting Ranitidine HCl matrix floating tablets showed fast floating regardless of media pH, robust performance, and sustained drug release in the stomach within a tight absorption window.[48]

The development of floating osmotic tablets containing Nizatidine, an H_2 receptor blocker, for the chronotherapeutic treatment of ulcers was reported by Bandameedi *et al* (2015). The three steps of the effervescence method were used to formulate the tablets: making floating sustained-release drug-containing tablets, coating them with ethyl cellulose (EC), a hydrophobic rupturable polymer, after a 4-hour lag time, and compression coating them with a buoyant layer and an immediate release dose of nizatidine. Here, ethyl cellulose and HPMC E15 was used in different ratios at different coating percentages ranging from 5-15%, were investigated in order to validate the 4-hour lag time. Sodium bicarbonate, carbopol 934P and cross-povidone were present in flexible layer. Further, Nizatidine formulation that was optimized demonstrated the intended two-phase release pattern, releasing the medication in the stomach for eight hours during the floating phase after an initial dose that was released in thirty minutes, followed by a four-hour lag period during which no drug release occurred.[49]

Conclusions

In summary, gastro-retentive floating drug delivery systems (GRFDDS) represent a promising approach to enhancing drug bioavailability and therapeutic efficacy. Advancements in formulation strategies, including the use of innovative polymers and gas-forming agents, have significantly improved the buoyancy and stability of these systems. The application of GRFDDS is particularly valuable for drugs with poor solubility or narrow absorption windows, making them essential in the management of various gastrointestinal conditions. In this review article, authors analyzed and compiled the published literature (2015-2023) dedicated towards gastro-retentive floating drug delivery systems. Despite the progress made, ongoing research is vital to address challenges such as scalability, patient compliance, and regulatory considerations. Future studies should focus on optimizing formulation parameters and exploring novel technologies to further advance the capabilities of GRFDDS, ultimately leading to more effective and personalized therapeutic solutions.

Acknowledgements

The authors declare their sincere thanks to Principal, Lord Shiva College of Pharmacy, Sirsa and Hon'ble Vice-chancellor, Guru Jambheshwar University of Science & Technology, Hisar for constant motivation and support.

Author contributions

SK conceptualized the article and wrote the original draft. JSC and HK contributed to reviewing, editing and supervision. RK and SD contributed for drafting, formatting and referencing of this manuscript. BN supported the complete work, helped in editing and as corresponding author for communicating with scientific esteemed journal having good reputation in the scientific fields.

Funding source

Authors declare that no external funding was received for the present work.

Competing interests

The authors declare no conflict of interest.

Ethical approval and consent to participate

Not applicable

References

1. Rajora A, Nagpal K. A Critical Review on Floating Tablets as a Tool for Achieving Better Gastric Retention. Critical Review in Therapeutic Drug Carrier Systems. 2022; 39(1):65-103. https://doi.org/10.1615/CritRevTherDrugCarrierSyst.2021038568 PMid:34936318

2. Neetika B, Manish G. Floating drug delivery system. International Journal of Pharmaceutical Research and Allied Sciences. 2012;1(4):20-28.

3. Ummadi S, Shravani B, Rao NR, Reddy MS, Sanjeev B. Overview on controlled release dosage form. International Journal of Pharma Sciences. 2013 Jun 26;7(8):51-60.

4. Awatade S, Bathe R, Mane S. Development and Evaluation of Floating Tablets of Pantoprazole. International Journal of Scientific in Science and Technology. 2019 Feb 24; 6(1):452-467. https://doi.org/10.32628/IJSRST196167

5. Ibrahim M, Naguib YW, Sarhan HA, Abdelkader H. Gastro-retentive Oral Drug Delivery Systems: A Promising Approach for Narrow

Absorption Window Drugs. Journal of Advanced Biomedical and Pharmaceutical Sciences. 2019 Jul 1;2(3):98-110.

6. Qi X, Chen H, Rui Y, Yang F, Ma N, Wu Z. Floating Tablets for Controlled Release of Ofloxacin via Compression Coating of Hydroxypropyl Cellulose Combined with Effervescent Agent. International Journal of Pharmaceutics. 2015 Jul 15;489(1-2):210-217. https://doi.org/10.1016/j.ijpharm.2015.05.007 PMid:25956047

7. Badoni A, Ojha A, Gnanarajan G, Kothiyal P. Review on Gastro Retentive Drug Delivery System. The Pharma Innovation. 2012 Oct 1;1(8, Part A):32.

8. Prajapati V.D, Jani G.K. Raft forming transfer: In vivo Evaluation and Implementation In In vitro and In Silico Predictive Tools. European Journal of Pharmaceutical Sciences. 2014 July 15;63:233-242. https://doi.org/10.1016/j.ejps.2014.07.008 PMid:25064697

9. Gunda RK, Vijayalakshmi A. Formulation Development and Evaluation of Gastro Retentive Drug Delivery Systems-A Review. Journal of Pharmacy Research. 2017 Feb 27;8(1):11-20.

10. Kandukoori NR, Shanthi MS, Sushma J, Ramya C, Swapna M, Madhu G, et al. A Review on Floating Drug Delivery System. World Journal of Pharmaceutical Research. 2017 Mar 14;6(5):553-568. https://doi.org/10.20959/wjpr20175-8451

11. Kothule S, Aher S, Bachhav R. Gastro-retentive Drug Delivery System: A Review. International Journal in Pharmaceutical Science. 2023 Feb 5;2(1):75-85.

12. Lodh H, Sheeba FR, Chourasia PK, Pardhe HA, Pallavi N. Floating Drug Delivery System: A Brief Review. American Journal of Pharmatech Research. 2020 July 8;10(4):255-264. https://doi.org/10.5958/2231-5713.2020.00043.4

13. Mahalakshmi GS, Anusha C, Bonthagarala B, Mohan M. Features and Facts of Gastro Retentive Floating Drug Delivery Systems-A Review. World Journal of Pharmaceutical research.2023 Feb 3;12(5):218-232.

14. Patole R, Chaware B, Mohite V, Redasani V. A Review for Gastro-Retentive Drug Delivery System. Asian Journal of Pharmaceutical Research and Development. 2023 Aug 13;11(4):79-94. https://doi.org/10.22270/ajprd.v11i4.1291

15. Shashank C, Prabha K, Sunil S, Vipin Kumar A. Approaches to Increase the Gastric Residence Time: Floating Drug Delivery Systems-A Review. Asian Journal of Clinical Research. 2013 May 24;6(3):1-9.

16. More S, Gavali K, Doke O, Kasgawade P. Gastro-retentive Drug Delivery System. Journal of Drug Delivery and Therapeutics. 2018 Jul 14;8(4):24-35. https://doi.org/10.22270/jddt.v8i4.1788

17. Jassal M, Nautiyal U, Kundlas J, Singh D. A review: Gastro-retentive drug delivery system (GRDDS). Indian Journal of Pharmaceutical and Biological Research. 2015 Jan 1;3(1):82-92. https://doi.org/10.30750/ijpbr.3.1.13

18. Dhole AR, Gaikwad PD, Bankar VH, Pawar SP. A Review on Floating Multiarticulate Drug Delivery System-A Novel Approach to Gastric Retention. International Journal of Pharmaceutical Sciences Review and Research. 2011 Jan 30;2(6): 205-211.

19. Katekar VA, Kothari PP, Nahar AA, Salve PA, Shendurkar HH, Adhau SA. A Review on Recent Advantages and Evaluation of Microparticles Aad Their Applications. GSC Biological and Pharmaceutical Sciences. 2023 Aug 22;24(2):297-307. https://doi.org/10.30574/gscbps.2023.24.2.0320

20. Mahalakshmi GS, Anusha C, Bonthagarala B, Mohan M. Features and Facts of Gastro Retentive Floating Drug Delivery Systems-A Review. World Journal of Pharmaceutical Research. 2023 Mar 14;12(5):218-232.

21. Kothule S, Aher S, Bachhav R. Gastro-retentive Drug Delivery System: A Review. International Journal in Pharmaceutical Sciences. 2023 Feb 5;1(2):75-85.

22. Tafish AM, Ebraheem AS, El Naggar EE, Elfar NN, Hamdy MY. Gastro-retentive drug delivery systems: A summarized overview. Octahedron Drug Research. 2023 May 29; 3(1): 40-56. https://doi.org/10.21608/odr.2023.209174.1027

23. Dwivedi A, Ghosal S, Kumar Mishra M, Bansal S, Dubey D. Evaluation of Mangifera Indica Gum as a Sustained Release Polymer in Glibenclamide Matrix Tablet. European Chemical Bulletin 2023 Jul 5;12(8):4098-4114.

24. Ranjeeth A, Parameshwar P. Formulation and Evaluation of Gastro Retentive Floating Matrix Tablets of Bilastine. Journal of Clinical Otorhinolaryngology, Head and Neck Surgery. 2023 Jan 30;27(2):587-603.

25. Wathore SA. Formulation and Evaluation of Lamivudine Extended-Release Floating Tablets by using HPMC Polymers and Xanthan Gum. International Journal of Pharmaceutical Research and Applications. 2023 May 8;8(3):262-273.

26. Rajput YS, Jaiswal R, Khan T. Preparation and Evaluation of Floating Tablet of Pantoprazole Sodium on Peptic Ulcer. International Journal of Pharmaceutical Research and Applications. 2022 Oct 10;7(5):1086-1095.

27. Gangwar S, Semwal N, Joshi D, Singh B. Development and Evaluation of Biodegradable Floating Drug Delivery for Solubility Enhancement of Diclofenac Sodium. World Journal of Biology Pharmacy and Health Sciences. 2022 Sep19;11(3):67-76. https://doi.org/10.30574/wjbphs.2022.11.3.0122

28. Mehetre GD, Chinchole PP, Narkhede MB. Formulation and Evaluation of a Hydrodynamically Balanced Gastro-retentive Drug Delivery System Incorporating Ciprofloxacin Hydrochloride. European Journal of Biomedical. 2022 Mar 13;9(4):283-288.

29. Kalita R, Kalita V, Bhattacharyya J. Formulation and Evaluation of Floating Matrix Tablet of Flurbiprofen. International Journal of Pharmaceutical Sciences and Drug Analysis. 2021 Mar 7;1(1):1-11.

30. Bakre LG, Akinyele E, Bamiro O, Adeleye O, Kunle O. Formulation and Evaluation of Sustained Release Ibuprofen Matrix Tablets using Starch from Maize Genotypes as Polymer. Acta Marisiensis-Seria Medica. 2021 May 31;67(2):122-126. https://doi.org/10.2478/amma-2021-0018

31. Singh VK, Sharma R, Rathi JC. Formulation Development and Evaluation of Bilayer Tablet for Effective Treatment of Gastric Ulcer. World Journal of Pharmaceutical Research. 2021 Mar 223;10(4):1373-1383. https://doi.org/10.38164/AJPER/10.4.2021.53-60

32. Lokeswara Babu V, Prajapati Sk. Formulation and Evaluation for Distribution of Free-Floating Matrix Tablets using in Anti-Parkinsonism. Journal of Critical Reviews. 2020 Feb 21;7(6):3049-3057.

33. Okafo SE, Alalor CA, Ordu JI. Design and In vitro Evaluation of Sustained Release Matrix Tablets of Metformin Produced using Detarium Microcarpum Gum. International Journal of Applied Pharmceutics. 2020 Jun 20;12(5):131-137. https://doi.org/10.22159/ijap.2020v12i5.38146

34. Vo AQ, Kutz G, He H, Narala S, Bandari S, Repka MA. Continuous Manufacturing of Ketoprofen Delayed Release Pellets using Melt Extrusion Technology: Application of QBD Design Space, Inline Near Infrared and Inline Pellet Size Analysis. Journal of Pharmaceutical Sciences. 2020 Dec 1;109(12):3598-3607. https://doi.org/10.1016/j.xphs.2020.09.007 PMid:32916139 PMCid:PMC7680423

35. Bhambar KV, Pande SD, Bhambar RS. Formulation and Evaluation of Floating Matrix Tablets of Drotaverine Hydrochloride. Journal of Drug Delivery and Therapeutics. 2019 May 15;9(3):200-206.

36. Eziuzo OS, Love II, Christian A. Formulation and Evaluation of Floating Matrix Tablets of Ciprofloxacin using Sida acuta Gum. Against Some Pathogenic Bacteria. International Journal of Drug Development & Research. 2019 Mar 27;8(11):4-8. https://doi.org/10.21767/0975-9344.1000128

37. Devi CM, Nath L, Laldinchana LL, Goswami A, Barakoti H. Formulation and Evaluation of Gastroretentive Floating Tablets of Diclofenac Sodium Based on Effervescent Technology.

International Journal of Pharmacy Biological Sciences. 2019 Jul 1;9(3):249-255.

38. Nagori S, Asija R, Gupta A, Garg A. Formulation and Evaluation of Sustained Release Matrix Tablets of Ketoprofen using Natural Gums. World Journal Pharmacy and Pharmaceutical Sciences. 2018 Jan 22;7(4):274-293.

39. Zhang J, Xu X, Zhu L, Fei X, Jin Z. Preparation and Pre-Clinical Characterization of Sustained-Release Ketoprofen Implants for the Management of Pain and Inflammation in Osteoarthritis. Tropical Journal of Pharmaceutical Research. 2018 Mar 20;17(4):577-582. https://doi.org/10.4314/tjpr.v17i4.2

40. Dumpa NR, Sarabu S, Bandari S, Zhang F, Repka MA. Chronotherapeutic Drug Delivery of Ketoprofen and Ibuprofen for Improved Treatment of Early Morning Stiffness in Arthritis using Hot-Melt Extrusion Technology. AAPS Pharm Sci Tech. 2018 Jul 2;19:2700-2709. https://doi.org/10.1208/s12249-018-1095-z PMid:29968041 PMCid:PMC6067978

41. Raza A. Bukhari NI, Karim S, Hafiz MA, Hayat U. Floating Tablets of Minocycline Hydrochloride: Formulation, In-Vitro Evaluation and Optimization. Future Journal of Pharmaceutical Sciences. 2017 May 3:3(2):131-139. https://doi.org/10.1016/j.fjps.2017.05.001

42. Vemula SK, Venisetty RK, Veerareddy PR. Valsartan Floating Bio Adhesive Compression-Coated Mini-Tablets: Formulation and Pharmacokinetics. Journal of Drug Delivery Science and Technology. 2017 Jun 3;40(1):66-72. https://doi.org/10.1016/j.jddst.2017.05.026

43. Rupavath M., Formulation, Optimization and in vitro Characterization of Stavudine Gastro-Retentive Floating Matrix Tablets. International Journal of Pharmaceutical and Drug Research. 2016 Jul 22;8(3):174-181. https://doi.org/10.25004/IJPSDR.2016.080309

44. Swain R. P. Formulation and evaluation of Gastro-bilayer Floating Tablets of Simvastatin as immediate Release Layer and Atenolol as Sustained Release Layer. International Journal of Pharmacy Biological Sciences. 2016 Jul 10;78(4):458-468. https://doi.org/10.4172/pharmaceutical-sciences.1000140

45. Kaleemullah M., Jiyauddin K., Thiban E., Rasha S., Al-Dhalli S., Budiasih S., Gamal O.E., et al. Development and Evaluation of Ketoprofen Sustained Release Matrix Tablet using Hibiscus Rosa-Sinensis Leaves Mucilage. Saudi Pharmaceutical Journal. 2017 Oct 7;25(5):770-779. https://doi.org/10.1016/j.jsps.2016.10.006 PMid:28725150 PMCid:PMC5506641

46. Ammar HO, Ghorab MM, Mahmoud AA, Noshi SH. Formulation of Risperidone in Floating Microparticles to Alleviate its Extrapyramidal Side Effects. Future Journal of Pharmaceutical Sciences. 2016 Dec 1;2(2):43-59. https://doi.org/10.1016/j.fjps.2016.08.001

47. Bera H, Gaini C, Kumar S, Sarkar S, Boddupalli S, Ippagunta SR. HPMC-Based Gastro-retentive Dual Working Matrices Coated with Ca+2 Ion Crosslinked Alginate-Fenugreek Gum Gel Membrane. Materials Science and Engineering: C. 2016 May 6;67:170-181. https://doi.org/10.1016/j.msec.2016.05.016 PMid:27287111

48. Kesarla RS, Vora PA, Sridhar BK, Patel G, Omri A. Formulation and Evaluation of Floating Tablet of H2-Receptor Antagonist. Drug Development and Industrial Pharmacy. 2015; 41(9):1499-1511. https://doi.org/10.3109/03639045.2014.959969 PMid:25243639

49. Bandameedi R, Pandiyan S. Formulation and Evaluation of Floating Osmotic Tablets of Nizatidine. Journal of Applied Pharmacy. 2015;7(4):1-7.