Floating Microspheres: An Innovative Approach for Gastric Retention

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ABSTRACT

Various scientific and technological attempts have been made in the development of gastroretentive dosage forms to overcome several physiological adversities, such as short gastric residence time, unpredictable gastric emptying time etc. These dosage forms can be retained in the stomach for prolonged period of time in a predetermined manner. Gastroretentive drug delivery technology is one of the promising approach for enhancing the bioavailability and controlled delivery of drugs that exhibit narrow absorption window. In pursuit of this endeavour, different novel strategies have been undertaken for the designing of several gastroretentive drug delivery systems including floating microspheres. This manuscript highlights various developmental approaches, characterization aspects, potential drug candidates along with diverse advantages and applications of floating microspheres. Numerous significant research findings in the vistas of these multiparticulates have also been described.

 Keywords: Gastroretentive technology, Floating microspheres, Bioavailability

INTRODUCTION

In recent years, drug delivery technology is becoming increasingly sophisticated as pharmaceutical scientists across the globe acquire a better understanding of the physicochemical and biological parameters related to the performance of various systems which enhances desirable therapeutic objectives while minimising side effects [1]. Despite significant advancements in drug delivery, oral route remains the preferred route for administration of several therapeutic agents due to improved patient compliance, ease of administration, flexibility in the design of formulation etc. [2]. Oral controlled release dosage forms have been extensively used to enhance therapy with better bioavailability. However, developmental process is hindered due to number of physiological adversities such as an
inability to restrain and localize the delivery system within the desired region of gastrointestinal tract [GIT], as well as fluctuation in gastric emptying and motility [2,3]. It can be anticipated that, depending upon the physiological state of subject and design of pharmaceutical formulation, the emptying process can last from few minutes to 12 h. This variability, in turn, may lead to unpredictable bioavailability and times to achieve peak plasma levels, since the majority of drugs are preferentially absorbed in upper part of the small intestine [4]. Furthermore, the relatively brief gastric emptying time in humans normally averages 2-3 h through the major absorption zone (stomach or upper part of the intestine) can result in incomplete drug release from the dosage form leading to diminished efficacy of administered dose. Thus, control over placement of drug delivery system in a specific region of the GI tract offers numerous advantages, especially for drugs exhibiting an absorption window in the GI tract or drugs with a stability problem. Overall, the intimate contact of drug delivery system with an absorbing membrane has potential to maximize drug absorption and may also influence the rate of drug absorption. These considerations have led to the development of oral controlled release dosage forms possessing gastric retention capabilities [5-7].

Gastroretentive drug delivery systems (GRDDS) can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention time (GRT) improves bioavailability, reduce drug waste and enhance solubility for drugs that are less soluble in high pH environment [8]. In the design and development of GRDDS, anatomical and physiological consideration of stomach also plays an important role [9]. Gastric retention can be achieved with the help of floating system, mucoadhesion or bioadhesion system, high density system, magnetic system, superporous hydrogels, raft forming system, low density system, floating ion exchange resins, unfoldable or expandable systems etc. Among the various approaches employed to increase the retention of an oral dosage form, floating drug delivery system is considerably easy and logical approach in the development of GRDDS [10-12].

**Floating Drug Delivery Systems**
These systems are intended to float in and over the gastric contents for an extended period of time [13,14]. Floating dosage units are useful for drugs acting locally and have a bulk density less than gastric fluids and so remain buoyant in the stomach for a prolonged period of time. While the system is floating over the gastric contents, the drug is released slowly at the desired rate from the system. This results in an increased GRT and better control of fluctuations in plasma drug concentration [2,15-17]. It is pertinent to note that presence of gastric content is needed to allow the proper achievement of buoyancy retention principle. Among different hydrocolloids recommended for floating formulations, cellulose ether polymers are most popular especially hydroxypropyl methylcellulose. Fatty materials with a bulk density lower than one may also be added to the formulations to increase the buoyancy [12,18,19].

**Design Considerations**
Floating units are useful for drugs which act locally in the proximal GIT. Because of the floating characteristics, these systems are valuable in retaining the dosage form in stomach for an extended period of time [20]. Following approaches have been used in the design of various floating dosage forms such as single- and multiple-unit dosage forms.
Single-Unit Dosage Forms

Single unit floating dosage forms such as floating tablets utilize matrices prepared with swellable polymers such as methocel, natural polysaccharides etc. and various effervescent components, e.g. sodium bicarbonate, citric acid and tartaric acid. These systems are fabricated so that upon contact with gastric fluid, carbon dioxide is liberated that is entrapped in the gellified hydrocolloid which produces an upward motion of the dosage form and maintains its buoyancy [12,21,22].

The success of Hydrodynamically balanced system (HBS) capsule as a better approach is also exemplified with several drugs. Moreover, these systems are designed to prolong the stay of dosage forms in the GIT and aid in enhancing the absorption. Such systems are best suited for drugs having a better solubility in acidic environment and also for the drugs having specific site of absorption in the upper part of small intestine. To remain in the stomach for a prolonged period of time, the dosage form must have a bulk density of less than unity. It should also stay in the stomach; maintain its structural integrity, and releases drug constantly from the dosage form. Fluid-filled floating chamber type of dosage forms includes incorporation of a gas filled floatation chamber into a microporous compartment that houses a drug reservoir. Apertures or openings are present along the top and bottom walls through which GIT fluid enters to dissolve the drug. Other two walls in contact with the fluid are sealed so that the undissolved drug remains therein. The device is of swallowable size, remains passes of the intestine, and is eliminated [21].

Also, bilayered tablets and self correcting floatable asymmetric configuration drug delivery system with 3-layer matrix technology have been shown to control the drug release with floatable characteristics. These dosage forms are variable in prolonging the GRT in the stomach when administered orally and are associated with problems such as sticking together or being obstructed in the GIT, which may have a potential danger of producing irritation [21, 23,24].

Multiple Unit Dosage Forms

Multiparticulate drug delivery technology represents frontier and promising avenue of pharmaceutical sciences which involves interdisciplinary scientific advancements in better health care along with improved therapeutic interventions [25]. Considerable research efforts have been undertaken in oral sustained or controlled release multiparticulate drug delivery system due to its advantages over single unit dosage forms [22]. After oral administration, multiple unit system retain their structure in GIT and each unit acts as an individual entity [26]. In pursuit of this endeavour, many multiple unit floatable dosage forms have been designed worldwide by large number of investigators [23]. Multiparticles can be developed in various forms such as granules, pellets, beads, mini-tablets, microspheres etc. [27]. With floating multiple unit dosage forms, it is considered that majority of particles will remain above the stomach contents for an extended period of time. This approach reduces the intersubject variability in absorption, lower the probability of dose dumping and bursting associated with the single-unit systems [21, 28-30]. It has also been described that multiple unit floating dosage forms distribute more uniformly with in the gastric content, resulting in long lasting effects [24]. These multiple units are low density systems that have sufficient buoyancy to float over gastric contents and remain in stomach for a prolonged period [31]. In these systems, dosage of the drug substance is divided on a plurality of subunit typically consisting of thousands of spherical particles. Furthermore, floating microspheres have high loading capacity and enormous synthetic and natural polymers have been widely employed in...
the developmental process which includes albumin, gelatin, starch, polymethacrylate, polyacrylamide and polycyanoacrylate. Spherical polymeric microsponges, also referred to “microballoons” have also been reported, moreover, microspheres have a characteristic internal hollow structure and showed an excellent in vitro floatability [23].

**Potential Drug Candidates**

Different drugs illustrate utmost therapeutic effect when releases in the stomach, particularly in a prolonged, continuous and controlled manner. Drugs delivered by this behaviour have a lower level of adverse effects and provide better therapeutic effects without the need of repeated dosage or with a low dosage frequency [32]. In general, appropriate candidates for controlled release gastroretentive dosage forms are molecules that have poor colonic absorption but are characterized by better absorption profile at the upper parts of the GIT. Various characteristics of the drugs which make them suitable for gastroretention approach are mentioned in the following text [2,33,34].

- Drugs those are locally active in the stomach e.g. misoprostol, antacids etc.
- Drugs that have narrow absorption window in GIT e.g. para aminobenzoic acid, furosemide, riboflavin etc.
- Drugs those are unstable in the intestinal or colonic environment e.g. captopril, ranitidine HCl, metronidazole.
- Drugs that disturb normal colonic microbes e.g. antibiotics against *Helicobacter pylori*.
- Drugs that exhibit low solubility at high pH values e.g. diazepam, chlordiazepoxide, verapamil HCl.
- Drugs that are primarily absorbed from stomach and upper part of GI tract e.g. calcium supplements, chlordiazepoxide, cinnarazine.

**Advantages of Floating Microspheres**

Recently, gastroretentive floating microspheres are gaining much more favour among various other dosage forms. Various potential benefits of these multiparticulate systems are presented in the following text [1,27,31,33,35-40].

- Improves patient comfort and compliance by decreasing dose frequency.
- Enhances the bioavailability and therapeutic efficacy of drugs with narrow absorption window in the upper part of GIT.
- Gastric retention time increases because of buoyancy principle.
- Drug releases in a controlled manner for prolonged period of time.
- Site-specific drug delivery can be achieved.
- Releases drug uniformly and there is no risk of dose dumping.
- Avoidance of gastric irritation, because of sustained release effect.
- Less inter- and intra-subject variability.
- Minimizes the counter activity of the body leading to higher drug efficiency.
- Fluctuations in drug concentration are minimized. Therefore, concentration dependent adverse effects can be reduced.
- Sustained mode of drug release enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcomes.
- Flexibility in dosage form design.
- Extend patent protection, globalize product, and provide new business opportunities.
Developmental Approaches
Wide ranges of developmental techniques are available for the preparation of gastroretentive floating microspheres [41]. However, solvent evaporation technique and ionotropic gelation method have been extensively employed by large number of scientific investigators worldwide to explore the different vistas of floating microspheres. During the preparation of floating controlled release microspheres, the choice of optimal method has utmost relevance for the efficient entrapment of active constituents. Selection of fabrication technique generally depends upon the nature of the polymer, the drug, and their intended use [42,43]. Characteristic features of materials and the process engineering aspects strongly influence the properties of microspheres and the resultant controlled release rate. These techniques (i.e. solvent evaporation and ionotropic gelation) are discussed in the subsequent section with pictorial representations (Figure 1 and Figure 2).

Solvent Evaporation Technique
This technique is widely employed by large number of pharmaceutical industries to obtain the controlled release of drug [44]. This approach involves the emulsification of an organic solvent (usually methylene chloride) containing dissolved polymer and dissolved/dispersed drug in an excess amount of aqueous continuous phase, with the aid of an agitator. The concentration of the emulsifier present in the aqueous phase affects the particle size and shape. When the desired emulsion droplet size is formed, the stirring rate is reduced and evaporation of the organic solvent is realized under atmospheric or reduced pressure at an appropriate temperature. Subsequent evaporation of the dispersed phase solvent yields solid polymeric microparticles entrapping the drug. The solid microparticles are recovered from the suspension by filtration, centrifugation, or lyophilisation [45]. For emulsion solvent evaporation, there are basically two systems which include oil-in-water (o/w) and water-in-oil (w/o) type.

Oil-In-Water Emulsion Solvent Evaporation Technique
In this process, both the drug and the polymer should be insoluble in water while a water-immiscible solvent is required for the polymer [46]. In this method, the polymer is dissolved in an organic solvent such as dichloromethane, chloroform, or ethyl acetate, either alone or in combination. The drug is either dissolved or dispersed into polymer solution and this solution containing the drug is emulsified into an aqueous phase to make an oil-in-water emulsion by using a surfactant or an emulsifying agent. After the formation of a stable emulsion, the organic solvent is evaporated either by increasing the temperature under pressure or by continuous stirring. Solvent removal from embryonic microspheres determines the size and morphology of the microspheres. It has been reported that the rapid removal of solvent from the embryonic microspheres leads to polymer precipitation at the o/w interface. This leads to the formation of cavity in microspheres, thus making them hollow to impart the floating properties [47-50]. Oil-in-water emulsion is widely used than water-in-oil due to simplicity of the process and easy cleans up requirement for the final product [51]. Schematic representation of this technique is shown in Figure 1.
Oil-in-Oil Emulsification Solvent Evaporation Technique
This oil-in-oil (sometimes referred as water-in-oil) emulsification process is also known as non aqueous emulsification solvent evaporation. In this technique, drug and polymers are co-dissolved at room temperature into polar solvents such as ethanol, dichloromethane, acetonitrile etc. with vigorous agitation to form uniform drug–polymer dispersion. This solution is slowly poured into the dispersion medium consisting of light/heavy liquid paraffin in the presence of oil soluble surfactant such as Span. The system is stirred using an overhead propeller agitator at 500 revolutions per minute (rpm) and room temperature over a period of 2–3 h to ensure complete evaporation of the solvent. The liquid paraffin is decanted and the microparticles are separated by filtration through a Whatmann filter paper, washed thrice with n-hexane, air dried for 24 h and subsequently stored in desiccator [52-56]. Span 60 is generally used which is non ionic surfactant. Span 60 has an HLB value of 4.3 and acts as a droplet stabilizer and prevents coalescence of the droplets by localizing at the interface between the dispersed phase and dispersion medium [54].

Ionotropic Gelation Method
In this method, cross linking of the polyelectrolyte takes place in the presence of counter ions to form gel matrix. This technique has been generally employed for the encapsulation of large number of drugs. Polyelectrolyte such as sodium alginate having a property of coating on the drug core and acts as release rate retardant contains certain anions in their chemical structure. These anions forms meshwork structure by combining with polyvalent cations and induced gelation. Microspheres are prepared by dropping drug loaded polymeric solution using syringe into the aqueous solution of polyvalent cations as depicted in Figure 2. The cations diffuses into the drug loaded polymeric drops, forming a three dimensional lattice of ionically cross linked moiety. Microspheres formed left into the original solution for sufficient time period for internal gelification and they are separated by filtration. Natural polymers such as alginates can be used to improve drug entrapment and are widely used in the development of floating microspheres [25,57-59].

Characterization Aspects
Characterization of floating microspheres is an important phenomenon which helps in the evaluation of suitable drug delivery systems. Floating microspheres are characterized by following parameters:

Particle size analysis
Particle size of floating microspheres is determined by using an optical microscopy and size
distribution is carried out by sieving method. This is useful in the determination of mean particle size with the help of calibrated ocular micrometer [60,61].

\[ \tan \theta = \frac{2H}{D} \]

where \( \theta \) is angle of repose, \( 2H/D \) is surface area of the free standing height of the microspheres heap that is formed on a graph paper after making the microspheres flow from glass funnel.

\textbf{Compressibility index}: Also called as Carr’s index and is computed according to the following equation:

\[ \text{Carr} \% = \frac{\text{Tapped density} - \text{Fluff density}}{\text{Tapped density}} \times 100 \]

\textbf{Hausner’s ratio}: Hausner’s ratio of floating microspheres is determined by comparing the tapped density to the fluff density using the equation:

\[ \text{Hausner’s ratio} = \frac{\text{Tapped density}}{\text{Fluff density}} \]

\textbf{Percentage yield}

Percentage yield of floating microspheres is calculated by dividing actual weight of product to total amount of all non-volatile components that are used in the preparation of floating microspheres and is represented by following formula: [65-67].
Drug entrapment efficiency
Estimation of drug content in floating microspheres can be carried out by dissolving the weighed amount of crushed microspheres in required quantity of 0.1 N HCl and analysed spectrophotometrically at a particular wavelength using the calibration curve. Each batch should be examined for drug content in a triplicate manner. The entrapment efficiency of floating microspheres is calculated by dividing the actual drug content by the theoretical drug content of microspheres [49,68,69].

Surface morphology
Surface characteristics of floating microspheres are analysed using a scanning electron microscopy. Samples are coated with gold dust under vacuum prior to observation. Cross sections should be made in order to observe the core and internal structure of the microspheres. These studies are useful in the examination of internal and external morphology of floating microspheres [70-72].

Swelling ratio
Swelling property of floating microspheres is studied by soaking the known weight of microspheres at 37 ± 0.5 °C in 0.1 N HCl or phosphate buffer pH 6.8 in a glass beaker for the required period of time. The microspheres are allowed to swell and removed at different time intervals. Their changes in weight are measured and calculated from the formula:

\[
\text{Swelling ratio} = \frac{W_e - W_o}{W_o}
\]

where, \(W_o\) is the initial weight of dry microspheres, \(W_e\) is the weight of swollen microspheres [72-74].

Buoyancy studies
In vitro floating tests can be performed in USP type II dissolution test apparatus by spreading the floating microspheres on a simulated gastric fluid (pH 1.2) containing the surfactant. The media is stirred at 100 rpm at 37± 0.5 °C. After specific intervals of time, both the fraction of microspheres (floating and settled microspheres) are collected and buoyancy of the floating microspheres is determined by using formula: [47,75].

\[
\text{Buoyancy} (%) = \frac{Q_f}{Q_f - Q_s} \times 100
\]

where, \(Q_f\) and \(Q_s\) are the masses of floating and settled hollow microspheres, respectively.

In vitro drug release studies
Release rate of drug from hollow floating microspheres is determined using USP dissolution apparatus type I or type II at 37± 0.5 °C. The dissolution test is carried out using 900 mL of 0.1 N HCl dissolution medium at 100 rpm for the required period of time. At an appropriate interval, specific volume of aliquots are withdrawn and replaced with an equivalent volume of fresh dissolution medium to maintain the constant volume of dissolution medium. The sample solutions are filtered through Whatman filter paper and solutions are analysed using
UV spectrophotometer [50,76].

**Significant research findings**

Concerted research efforts have been carried out worldwide to explore the different vistas of floating microspheres. Significant numbers of innovations and advancements have been done with floating microspheres and are presented in the table 1.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>POLYMER(S)</th>
<th>METHOD</th>
<th>REFERENCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol,</td>
<td>Eudragit S100</td>
<td>Solvent diffusion</td>
<td>[48]</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Eudragit S 100, Eudragit RL</td>
<td>Emulsion solvent diffusion</td>
<td>[49]</td>
</tr>
<tr>
<td>Silymarin</td>
<td>HPMC, Ethyl cellulose</td>
<td>Solvent diffusion-evaporation</td>
<td>[50]</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>Eudragit RS 100, Ethyl cellulose</td>
<td>Non-aqueous emulsification solvent evaporation</td>
<td>[53]</td>
</tr>
<tr>
<td>maleate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem HCl</td>
<td>Ethyl cellulose</td>
<td>Solvent evaporation</td>
<td>[54]</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Propyl dextran mixture ester</td>
<td>Emulsion solvent evaporation</td>
<td>[55]</td>
</tr>
<tr>
<td>Diltiazem HCl</td>
<td>Sodium alginate, Chitosan, Eudragit RS30D</td>
<td>Ionotropic gelation method</td>
<td>[57]</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Xanthan gum, Gelatin</td>
<td>Emulsification</td>
<td>[60]</td>
</tr>
<tr>
<td>Aceclofenac</td>
<td>Eudragit RS100</td>
<td>Emulsification solvent evaporation</td>
<td>[64]</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>Eudragit S</td>
<td>Emulsion solvent diffusion</td>
<td>[65]</td>
</tr>
<tr>
<td>Diltiazem HCl</td>
<td>HPMC, Ethyl cellulose</td>
<td>Nanoprecipitation</td>
<td>[66]</td>
</tr>
<tr>
<td>Propranolol HCl</td>
<td>Chitosan</td>
<td>Chemical denaturation</td>
<td>[68]</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Eudragit RL100, Cellulose acetate butyrate</td>
<td>Emulsion solvent evaporation</td>
<td>[71]</td>
</tr>
<tr>
<td>Diclofenac sodium</td>
<td>Eudragit S100</td>
<td>Emulsion solvent diffusion</td>
<td>[75]</td>
</tr>
<tr>
<td>Acyclovir</td>
<td>Eudragit S100</td>
<td>Emulsion solvent evaporation diffusion</td>
<td>[76]</td>
</tr>
<tr>
<td>Josamycin</td>
<td>Eudragit E100</td>
<td>Solvent diffusion and evaporation</td>
<td>[77]</td>
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<td>Tranilast,</td>
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<td>[78]</td>
</tr>
<tr>
<td>Ibuprofen</td>
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<td></td>
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</tr>
<tr>
<td>Cimetidine</td>
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<td>Solvent evaporation</td>
<td>[79]</td>
</tr>
<tr>
<td>Famotidine</td>
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<td>Piroxicam</td>
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<td>[81]</td>
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<td>Theophylline</td>
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<td>Orlistat</td>
<td>Eudragit S</td>
<td>Solvent evaporation</td>
<td>[83]</td>
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</tbody>
</table>
### Salient applications:
Floating microspheres are potential drug delivery systems with diverse advantages and variety of pharmaceutical applications. These are particularly advantageous for drugs with poor bioavailability because of narrow absorption window in the upper part of GIT. These systems retain the dosage form at the site of absorption and thus enhance the bioavailability. Some important examples are discussed in the following text [5,8, 31,36,37,40,47,78,90,97,102-104].

<table>
<thead>
<tr>
<th>Drug</th>
<th>Excipients/Methods</th>
<th>Refs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin HCl</td>
<td>Ethyl cellulose</td>
<td>[84]</td>
</tr>
<tr>
<td>Aspirin, Indomethacin</td>
<td>Eudragit S100, Eudragit L100, Eudragit L100-55, Ethyl cellulose</td>
<td>[85]</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>Eudragit S100</td>
<td>[86]</td>
</tr>
<tr>
<td>Piroxicam, Ketoprofen</td>
<td>Polycarbonate, Eudragit S100, Eudragit RL</td>
<td>[87]</td>
</tr>
<tr>
<td>Nicardipine HCl, Dipyridamole</td>
<td>Cellulose acetate</td>
<td>[89]</td>
</tr>
<tr>
<td>Acetohydroxamic acid</td>
<td>Eudragit E, Polycarbophil</td>
<td>[90]</td>
</tr>
<tr>
<td>Cefpodoxime proxetil</td>
<td>HPMC K4M, HPMC K100LV, Ethyl cellulose</td>
<td>[91]</td>
</tr>
<tr>
<td>Ketorolac trometamol</td>
<td>Eudragit R100, Eudragit S100, HPMC K4M, Ethyl cellulose</td>
<td>[92]</td>
</tr>
<tr>
<td>Cefpodoxime proxetil</td>
<td>HPMC K15M, Ethyl cellulose</td>
<td>[93]</td>
</tr>
<tr>
<td>Glipizide</td>
<td>HPMC, Ethyl cellulose</td>
<td>[94]</td>
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<td>Cinnarizine</td>
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<td>[95]</td>
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<td>Verapamil HCl</td>
<td>Eudragit S100, Cellulose acetate, Acrycoat S100</td>
<td>[96]</td>
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<tr>
<td>Ranitidine HCl</td>
<td>Ethyl cellulose</td>
<td>[97]</td>
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<td>Famotidine</td>
<td>Polymethylmethacrylate, Ethyl cellulose</td>
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<tr>
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<td>Acrycoat S100, Cellulose acetate</td>
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<tr>
<td>Aspirin, Riboflavin</td>
<td>Eudragit S 100</td>
<td>[100]</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Cellulose acetate</td>
<td>[101]</td>
</tr>
</tbody>
</table>

Scholar Research Library
Gastroretentive floating microspheres are very effective in the reduction of major adverse effect of gastric irritation; such as floating microspheres of non-steroidal anti-inflammatory drugs i.e. indomethacin are beneficial for rheumatic patients.

Floating microspheres can greatly improve the pharmacotherapy of stomach through local drug release. Thus, eradicating *Helicobacter pylori* from sub-mucosal tissue of the stomach are useful in the treatment of peptic ulcers, chronic gastritis, gastro-oesophageal reflux diseases etc. Floating bioadhesive microspheres of acetohydroxamic acid are formulated for treatment of *Helicobacter pylori* infection. Hollow microspheres of ranitidine HCl are also developed for the treatment of gastric ulcer.

These microparticulate systems provide sustained drug release behaviour and release the drug over a prolonged period of time. Hollow microspheres of tranilast are fabricated as a floating controlled drug delivery system.

Floating microspheres are very effective approach in delivery of drugs that have poor bioavailability because of their limited absorption in the upper GIT. These systems efficiently maximize their absorption and improve the bioavailability of several drugs. e.g furosemide, riboflavin etc.

**CONCLUSION**

Gastroretentive floating drug delivery technology has emerged as an efficient approach for enhancing the bioavailability and controlled delivery of various therapeutic agents. Significant attempts have been made worldwide to explore these systems according to patient requirements, both in terms of therapeutic efficacy and compliance. Floating microspheres as gastroretentive dosage forms precisely control the release rate of target drug to a specific site and facilitates an enormous impact on health care. Optimized multi-unit floating microspheres are expected to provide clinicians with a new choice of an economical, safe and more bioavailable formulation in the effective management of diverse diseases. These systems also provide tremendous opportunities in the designing of new controlled and delayed release oral formulations, thus extending the frontier of futuristic pharmaceutical development. Increased sophistication of this technology will ensure the successful advancements in the avenue of gastroretentive microspheres therapy so as to optimize the delivery of molecules in a more efficient manner. Furthermore, recent innovations in pharmaceutical investigation will surely provide real prospects for establishment of novel and effective means in the development of these promising drug delivery systems.

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