INDO AMERICAN JOURNAL OF PHARMACEUTICAL RESEARCH

FLOATING MULTIPARTICULATE SYSTEMS: A NOVEL APPROACH IN GASTRORETENTIVE DRUG DELIVERY SYSTEMS

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ARTICLE INFO

Article history
Received 03/03/2017
Available online
2017

Keywords
Floating,
Multiparticulate Systems,
Microspheres,
Beads,
Granules.

ABSTRACT

Recent advances in novel drug delivery system to enhance the safety and efficacy of the drug molecule by formulating a dosage form being convenient for administration. A controlled drug delivery system with prolonged residence time in the stomach can be of great practical importance for drugs with an absorption window in the upper small intestine. The main limitations are attributed to the inter- and intra-subject variability of gastro-intestinal (GI) transit time and the non-uniformity of drug absorption throughout the alimentary canal. Floating drug delivery systems (FDDSs) are expected to remain buoyant in a lasting way upon the gastric contents and consequently to enhance the bioavailability of drugs. The various buoyant preparations include hollow microspheres, granules, beads and powders. Multiparticulate low-density particles can successfully prolong the gastric retention time of drugs. This article is a review of important approaches utilized in the preparation of floating multiparticulate systems, characterization of floating multiparticulate systems and recent research work done on floating multiparticulate systems.

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*Please cite this article in press as **Dr. R. Santosh Kumar** et al. Floating Multiparticulate Systems: A Novel Approach in Gastroretentive Drug Delivery Systems. Indo American Journal of Pharmaceutical Research.2017:7(03).*

INTRODUCTION

Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Several difficulties are faced in designing controlled release systems for better absorption and enhanced bioavailability. One of such difficulties is the inability to confine the dosage form in the desired area of the gastrointestinal tract (GIT). Drug absorption from the GIT is a complex procedure and is subject to many variables. It is widely acknowledged that the extent of gastrointestinal drug absorption is related to contact time with the small intestinal mucosa.[1,2] Although single unit floating dosage forms have been extensively studied, these single unit dosage forms have the disadvantage of a release all or nothing during emptying process while the multiple unit particulate system pass through the GIT to avoid the vagaries of gastric emptying and thus release the drug more uniformly. The uniform distribution of these multiple unit dosage forms along the GIT could result in more reproducible drug absorption and reduced risk of local irritation; this gave birth to oral controlled drug delivery and led to development of gastro-retentive floating microspheres, floating beads and floating granules.[3,4,5]

The purpose of designing multiple-unit dosage form is to develop a reliable formulation that has all the advantages of a single-unit form and also is devoid of any of the above mentioned disadvantages of single unit formulations. In pursuit of this endeavor many multiple-unit floatable dosage forms have been designed. Microspheres have high loading capacity and many polymers have been used such as albumin, gelatin, starch, polymethacrylate, polyacrylamine, and polyalkylcyanoacrylate. Spherical polymeric microsponges also referred to as "microballoons," have been prepared. Microspheres have a characteristic internal hollow structure and show an excellent in vitro floatability.[5] In carbon dioxide– generated multiple-unit oral formulations, several devices with features that extend, unfold, or are inflated by carbon dioxide generated in the devices after administration have been described in the recent patent literature. These dosage forms are excluded from the passage of the pyloric sphincter if a diameter of ~12 to 18 mm in their expanded state is exceeded.[6,7] Multiparticulate carriers (microspheres) are defined as homogeneous, monolithic particles in the size range of about 0.1-1000µm and are widely used as drug carriers for controlled release. Multiparticulate carrier systems made from the naturally occurring biodegradable polymers have attracted considerable attention for several years in sustained drug delivery.

Recently dosage forms that can precisely control the release rates and target drugs to a specific body site have created enormous impact in formulation and development of novel drug delivery systems. Microspheres form an important part of such novel drug delivery systems. They have varied applications and are prepared using various polymers. However, the success of these microspheres is limited due to their short residence time at the site of absorption. It would, therefore be advantageous to have means for providing an intimate contact of the drug delivery system with the absorbing membranes. This can be achieved by coupling gastro retentive and bioadhesion characteristics to multiparticulates and developing gastro retentive bioadhesive multiparticulates. These multiparticulates have advantages like efficient absorption and enhanced bioavailability of the drugs due to a high surface to volume ratio, a much more intimate contact with the mucus layer and specific targeting of drugs to the absorption site. [8]

Drug Candidates for Gastro Retentive Delivery Systems

1. Drugs those are locally active in the stomach
e.g. Misoprostol, antacids etc.
2. Drugs that have narrow absorption window in gastrointestinal tract (GIT)
e.g. L-DOPA, para amino benzoic acid, furosemide, riboflavin etc.
3. Drugs those are unstable in the intestinal or colonic environment
e.g. Captopril, ranitidine HCl, metronidazole.
4. Drugs that disturb normal colonic microbes
e.g. Antibiotics against Helicobacter pylori.
5. Drugs that exhibit low solubility at high pH values
e.g. Diazepam, chlordiazepoxide, verapamil hydrochloride

Methods of Preparation of Gastro-Retentive Multiparticulate System

Solvent Evaporation Method

Floating multiparticulate dosage form can be prepared by solvent diffusion and evaporation methods to create the hollow inner core. The polymer is dissolved in an organic solvent and the drug is either dissolved or dispersed in the polymer solution. The solution containing the drug is then emulsified into an aqueous phase containing suitable additive (surfactants / polymer) to form oil in water emulsion. After the formation of a stable emulsion, the organic solvent is evaporated either by increasing the temperature under pressure or by continuous stirring.[9],[10] The solvent removal leads to polymer precipitation at the oil/water interface of droplets, forming cavity and thus making them hollow to impart the floating properties. The polymers studied for the development of such systems include cellulose acetate, chitosan, Eudragit, Acrycoat, Methocil, polyacrylates, polyvinyl acetate, carbopol, agar, polyethylene oxide and polycarbonates.[11]

Ionotropic Gelation Method

Ionotropic gelation is based on the ability of poly electrolytes to cross link in the presence of counter ions to form beads. Since, the use of alginates, gellan gum, chitosan and carboxymethyl cellulose for the encapsulation of drug and even cells, ionotropic gelation technique has been widely used for this purpose.[12] The natural poly electrolytes in spite, having property of coating on the drug core and acts as release rate retardants contains certain anions on their chemical structure. These anions forms meshwork structure by combining with the polyvalent cations and induce gelation by binding mainly to the anion blocks. The hydrogel beads are produced by dropping a drug-loaded polymeric solution into the aqueous solution of polyvalent cations. [13]

Emulsion Solvent Diffusion Method

In the emulsion solvent diffusion method the affinity between the drug and organic solvent is stronger than that of organic solvent and aqueous solvent. The drug is dissolved in the organic solvent and the solution is dispersed in the aqueous solvent producing the emulsion droplets even though the organic solvent is miscible. The organic solvent diffuse gradually out of the emulsion droplets in to the surrounding aqueous phase and the aqueous phase diffuse in to the droplets by which drug crystallizes.

Novel Method for Foam Powder

Furthermore, a novel multi-particulate gastroretentive drug delivery system based on low-density foam powder has been proposed and its performance demonstrated *in vitro*.[14] Floating microparticles consisting of polypropylene foam powder, verapamil hydrochloride (as the model drug) and Eudragit RS, ethyl cellulose or poly (methyl methacrylate) were prepared with an oil-in water solvent extraction / evaporation method. The drug and release rate - controlling polymer were dissolved in methylene chloride. Polypropylene foam powder was then dispersed within this organic phase. The resulting suspension was subsequently emulsified into an external aqueous poly (vinyl alcohol) solution and agitated with a stirrer to allow microparticle formation. The microparticles were separated by being sieved, washed with water and dried in desiccator they were irregular in shape and highly porous. Importantly, the drug encapsulation efficiency was high and almost independent of the theoretical loading of the system. In all cases, good *in-vitro* floating behavior was observed. Interestingly, a broad spectrum of release patterns could be obtained with the investigated formulations. Further studies focused on the development of an improved preparation method for this type of low density, foam-based, floating microparticle and also on the demonstration of the system's performances *in vitro*.[15] Major advantages of the suggested novel preparation technique include short processing times, no exposure of the ingredients to high temperatures, the ability to avoid toxic organic solvents and high encapsulation efficiencies. Floating microparticles consisting of polypropylene foam powder, model drug (chlorpheniramine maleate, diltiazem hydrochloride, theophylline or verapamil hydrochloride) and a second polymer [Eudragit RS or Poly(methyl methacrylate)] were prepared by soaking microporous foam particles with an organic solution of the drug and polymer and subsequent drying (Figure 2).[16] Good *in- vitro* floating behavior was observed in most cases and a broad variety of drug release patterns could be achieved by varying the drug loading and type of second polymer.[17]

Melt Granulation Technique

Melt granulation is processes by which granules are obtained through the addition of either a molten binder or a solid binder which melts during the process. This process is also called melt agglomeration and thermoplastic granulation. [18,19,20,21]

Principle of Melt granulation:

The process of granulation consists of a combination of three phases:
I. Wetting and nucleation,
II. Coalescence step,
III. Attrition and breakage.

Wetting and Nucleation Step:

During the nucleation step the binder comes into contact with the powder bed and some liquid bridges are formed, leading to the formation of small agglomerates. Two nucleation mechanisms are proposed by mSchafer and Mathiesen.
I. Immersion
II. Distribution

Immersion

• Nucleation by immersion occurs when the size of the molten binder droplets is greater than that of the fine solid particles.
• Immersion proceeds by the deposition of fine solid particles onto the surfaces of molten binder droplets.

Distribution

• In the distribution method a molten binding liquid is distributed onto the surfaces of fine solid particles.
• The nuclei are formed by the collision between the wetted particles.
• Generally, small binder droplet size, low binder viscosity, and high shearing forces are favorable conditions for nucleation by the distribution method.

Coalescence step:
• It involves nuclei that have residual surface liquid to promote successful fusion of nuclei.
• The surface liquid imparts plasticity to the nuclei and is essential for enabling the deformation of nuclei surface for coalescence as well as promoting the rounding of granulation.

Attrition-breakage step:
• Attrition and breakage refer to the phenomenon of granulation fragmentation in that are solidified by tray cooling to ambient temperature without the need for drying by a tumbling process.
• Consequently, breakage is known to have a more essential role in affecting the resultant properties of the melt granulation during the granulation phase.

Requirements of Melt granulation:
• Generally, an amount of 10–30% w/w of meltable binder, with respect to that of fine solid particles, is used.
• A meltable binder suitable for melt a granulation has a melting point typically within the range of 50–100 C.
• Hydrophilic meltable binders are used to prepare immediate-release dosage forms while the hydrophobic meltable binders are preferred for prolonged-release formulations.
• The melting point of fine solid particles should be at least 20°C higher than that of the maximum processing temperature.

Meltable Binders:
• It must be solid at room temperature and melt between 40 and 80°C,
• Its physical and chemical stability
• Its hydrophilic-lipophilic balance (HLB) to ensure the correct release of the active substance.
There are two type of Meltable binder:
1) Hydrophilic meltable binders
2) Hydrophobic meltable binder

Advantages of Melt granulation:
• Neither solvent nor water used.
• Fewer processing steps needed thus time consuming drying steps eliminated.
• Uniform dispersion of fine particle occurs.
• Good stability at varying pH and moisture levels.
• Safe application in humans due to their non swellable and water insoluble nature.

The melt granulation process carries several advantages over conventional pharmaceutical granulation methods, as the process does not require the use of solvents. A further significant advantage of melt granulation is that judicious choice of the granulation excipient may enable the formulator to manipulate the drug dissolution rate from the corresponding dosage form. The melt granulation process uses substances that melt at relatively low temperature (i.e., 50-80 C). These substances can be added to the molten form over the substrate or to a solid form, which is then heated above its melting points by hot air or by a heating jacket. In both cases, the substance acts like a liquid binder after it melts. Thus melt granulation does not require the organic or aqueous solvents. Moreover the drying step is not necessary in melt granulation, thus the process is less time consuming and more energy efficient than wet granulation. After selecting a suitable binder, one can use melt granulation to prepare controlled release or improved release granules. Polyoxyl stearates may be considered as potentially useful hydrophilic binders in melt granulation. When water soluble binders are needed, Polyethylene Glycol (PEG) is used as melting binders. When water insoluble binders are needed, Stearic acid, cetyl or stearyl alcohol, various waxes and mono-, di-, & triglycerides are used as melting binders.

Types of Gastroretentive Multiparticulate Drug Delivery System
Floating Beads

Floating beads can be prepared using the polymers having a property of ionotropic gelation like sodium alginate and pectin. The spherical beads in the size range of 1-2.5 mm in diameter can be prepared by dropping the aqueous solution containing polymer and drug in to an aqueous solution of calcium chloride, causing precipitation of polymer in presence of calcium ions. The beads are then separated and dried for suitable time to attain constant weight. The beads can be made buoyant by adding sodium bicarbonate or mineral oil in to the polymer solution during the preparation of beads. The oil added during the preparation is entrapped in to the beads which lowers the density of the beads and cause them to float. The bicarbonate generates carbon dioxide (CO_2) that entraps in the beads thereby lowering the density of the beads and leading to floating. The literature review on different methods used by researchers is shown in Table 1.1. [22-35]

Table 1.1: Floating Beads.

Researcher	Drug used	Method used	Polymer used	Achievements
Jaiswal et al.[18]	Ranitidine hydrochloride	Emulsion Gelation	Sodium alginate, Pectin	Beads entrapped even a water soluble drug as ranitidine HCL in sufficient amount and also can successfully deliver the drug in stomach for a prolong duration of time.
Mishara et al.[19]	Loratidine	Emulsion Gelation	Sodium alginate, pectin, ethyl cellulose	Controlled release formulation of loratidine provided zero-order release for 8 h.
Tripathi et al.[20]	Clarithromycin	Ionic gelation	Pectin, ethyl Cellulose	The formulation exhibited sustained release profile and was best fitted to the Peppas model with n < 0.45.
Vidyasagar et al.[21]	Clarithromycin	Emulsion Gelation	Sodium alginate, hydroxy propyl methyl cellulose (HPMC)	In-vitro dissolution studies reveals that this formulation gave sustained release pattern of clarithromycin up to12 hr.
Mandal et al.[22]	Furosemide	Emulsiongelation	Sodium alginate	A higher level of oil increased drug entrapment efficiency but retarded drug release rate as compared to a lower level of oil containing beads.
Vedha et al.[23]	Nevirapine	Ionic gelation	Sodium alginate, hydroxypropyl methylcellulose	The beads containing higher amounts of calcium carbonate demonstrated an instantaneous, complete, and excellent floating ability over a period of 24 hr.
Mishra et al.[24]	Acetohydroxamic acid (AHA)	Ionotropic Gelation	Gellan gum	Oral dosage form of floating gella beads containing AHA may form a useful stomach site specific drug delivery system for the treatment of *H. pylori* infection.
Shishu et al.[25]	5-flurouracil (5-FU)	Ionic gelation	Sodium alginate and hydroxypropyl methylcellulose	The beads containing higher amounts of calcium carbonate demonstrated instantaneous, complete, and excellent floating ability over a period of 24hr.
Verma et al.[26]	Rifabutin	Ionotropic	Gellan gum	The beads exhibited excellent buoyancy in simulated gastric fluid (SGF) and remained buoyant for 18 hr.
Kouchaka et al.[27]	Diclofenac	Ion exchange	Ethyl cellulose, Eudragit RS-100	Ethyl cellulose-coated beads have a desirable floating capability in comparison with the Eudragit RS-100 coated beads.
Vani et al.[29]	Ranitidine hydrochloride	Extrusion congealing	HPMC, sodium alginate	Study revealed that the gastro retentive drug delivery system designed as floating beads could be suitable drug delivery system for ranitidine hydrochloride.
Somani et al.[30]	Aceclofenac	Ionotropic	Crosslinking Pectin Calcium pectinate	microparticles as a promising floating pulsatile drug delivery for site and time specific release of drug acting as per the chronotherapy of disease.
Sriamornsak et al.[31]	Metronidazole	Modified emulsion gelation	Pectin	The study revealed that as the amount of incorporated wax increased in the formulation significantly sustained the drug release while beads remaining floating.

Floating Microspheres

Floating microspheres are gastro-retentive drug delivery systems based on non-effervescent approach. Hollow microspheres are in strict sense, spherical empty particles without core. These microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, ideally having a size less than 200µm. Solid biodegradable microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for controlled release of drugs. Gastro-retentive floating microspheres are low density systems that have sufficient buoyancy to float over gastric contents and remain in stomach for prolonged period. As the system floats over gastric contents, the drug is released slowly at desired rate resulting in increased gastric retention with reduced fluctuations in plasma drug concentration.[36] The literature review on different methods used by researcher's is shown in Table.1. 2.[37-52]

Table.1.2. Floating Microspheres.

Researcher	Drug used	Method used	Polymer used	Achievements
Jain et al.[33]	Orlistat	Solvent evaporation	Calcium silicate	Prolonged gastric residence time of over 6 hours was achieved in all rabbits for calcium silicate based floating microspheres of Orlistat.
Punitha et al.[34]	Ranitidine hydrochloride	Solvent evaporation	HPMC K15M,	The present novel drug – floating microsphere approach for ranitidine HCL proposed that with both acrylic and hydrophilic polymers the GI retention can be enhanced.
Srivastava et al.[35]	Cimetidine	Solvent evaporation	HPMC, ethyl cellulose	In vitro studies demonstrated diffusion controlled drug release from the microspheres.
Tanwar et al.[36]	Verapamil hydrochloride	Diffusion evaporation	Cellulose acetate, Acrycoat S100, Eudragit S100	The prepared microspheres exhibited prolonged drug release and remained buoyant for more than 12 h.
Reddy et al.[37]	Cyclobenzaprine hydrochloride	Emulsion solvent diffusion	Ethyl cellulose	EC microsphere retain in upper GIT and there by improved bioavailability.
Gattani et al.[39]	Aceclofenac	Solventevaporation	Eudragit RS	The prepared microspheres exhibited prolonged drug release (>12hr) and remained buoyant.
Pandey et al.[40]	Famotidine	Solvent evaporation	HPMC, ethyl cellulose	Study revealed that floating microspheres of famotidine may be used in clinic for prolonged drug release in stomach for at leat 12hr, there by improving the bioavailability and patient compliance.
Garg et al.[41]	Silymarin	Emulsionsolvent evaporation	HPMC, ethyl cellulose (EC) ,Eudragit® S 100 (ES), Eudragit® RL (ERL)	The microspheres exhibited prolonged drug release for 12 h while still remained buoyant.
Fartyal et al.[42]	Boswellic acid	Solvent evaporation	HPMC, ethyl cellulose	The prepared microspheres exhibited prolonged drug release (18h) and remained buoyant for > 12 h.
Najmuddin et al.[43]	Ketoprofen	Emulsion solvent diffusion	Eudragit S 100, Eudragit L 100	Floating microspheres of ketoprofen are promising for sustained drug delivery which can reduce dosing frequency.
Patel et al.[44]	Glipizide	Emulsification phase separation	Chitosan	The drug release was sustained for more than 12 h. *In-vivo* testing of the mucoadhesive microspheres to Albino Wistar rats demonstrated significant Hypoglycaemic effect of glipizide.
Naggar et al.[45]	Ketoprofen	Emulsion solvent diffusion	Eudragit S100 (ES), Eudragit RL (ERL).	The formulation containing ES:ERL (1:1) exhibited high percentage of floating particles in all examined media.
Kawashima et al.[46]	Tranilast	Emulsionsolvent diffusion	Acrylic polymers	An in vivo radiographical study proved that microballoons orally administered to humans were dispersed in the upper part of the stomach and retained there for over 3 h against peristaltic action.

Barhate et al.[47]	Ketorolac trometamol	Emulsion solvent diffusion	Ethyl cellulose, HPMC K4M, Eudragit R 100, Eudragit S 100	The optimized formulation shows good buoyancy and *in vitro* controlled release of ketorolac trometamol.
Yasunori et al.[48]	Aspirin, Salicylic acid, ethoxybenzamide, indomethacin, riboflavin	solvent diffusion	Enteric acrylic polymers	The release properties of five different drugs exhibiting distinct water solubilities (aspirin, salicylic acid, ethoxybenzamide, indomethacin, riboflavin entrapped within microballoons were investigated.

Floating Granules

Multi unit dosage from such as granules or pellets may be more suitable because they claim to reduce the intersubject variability in absorption and lower the probability of dose dumping.[53] Floating granule can be prepared using a drug with suitable lipophilic polymer having low density. The polymers used for these granules are usually meltable at moderate temperature allowing the use of solvent free melt granulation technology for granulation.The literature review on different methods used by researchers is shown in Table 3. [54,55]

Table. 1.3 Floating Granules.

Researcher	Drug used	Method used	Polymer used	Achievements
Patel et al.[50]	Ranitidine hydrochloride	Melt granulation	Gelucire 43/01	The study indicated that the hydrophobic lipid Gelucire 43/01 can be considered as a effective carrier or design of a multiple unit floating drug delivery system for highly water soluble
Shimpi et al.[51]	Diltiazem hydrochloride	Melt granulation	Gelucire 43/01	Study revealed that hydrophobic lipid, Gelucire 43/01, can be considered as an effective carrier for design of a multi-unit floating drug delivery system of highly water-soluble drugs such as diltiazem hydrochloride.

Characterization of Gastroretentive Multiparticulate System Micromeritic Properties

Angle of repose, density, hausner's ratio, compressibility index is determined by using proper equations.[56,57]

Particle Size and Shape

Scanning electron microscopy (SEM) provides higher resolution in contrast to the light microscopy (LM). The most widely used procedures to visualize microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM). Both can be used to determine the shape and outer structure of multiparticulate. LM provides a control over coating parameters in case of double walled microspheres. The multiparticulate structures can be visualized before and after coating and the change can be measured microscopically. SEM allows investigations of the multiparticular surfaces and after particles are cross sectioned, it can also be used for the investigation of double walled systems. Conflocal fluorescence microscopy is used for the structure characterization of multiple walled microspheres. Laser light scattering and multi size coulter counter other than instrumental methods, which can be used for the characterization of size, shape and morphology of the multiparticulate. [58]

Entrapment Efficiency

The capture efficiency of the multiparticulate or the percent entrapment can be determined by allowing washed multiparticulate to lyse. The lysate is then subjected to the determination of active constituents as per monograph requirement. The percent encapsulation efficiency is calculated using equation: % Entrapment = Actual content/Theoretical content x 100

Floating Behavior

Appropriate quantity of the floating microparticulate is placed in 100 ml of the simulated gastric fluid (SGF, pH 2.0), the mixture is stirred with a magnetic stirrer. The layer of buoyant microparticulate is pipetted and separated by filtration. Particles in the sinking particulate layer are separated by filtration. Particles of both types are dried in a desiccator until constant weight is achieved. Both the fractions of microspheres are weighed and buoyancy is determined by the weight ratio of floating particles to the sum of floating and sinking particles. Buoyancy (%) = W_f / W_f + Ws. Where, W_f and Ws are the weights of the floating and settled microparticles.[55]

***In Vitro* Release Studies**

The release rate of floating microparticulate is determined in dissolution apparatus. A weighed amount of floating microspheres equivalent to dose of drug is taken and placed in the basket of dissolution rate apparatus. The dissolution fluid is maintained at 37 ± 0.5°C at a rotation speed that provides sink conditions during the drug release study. [56]

***In Vivo* Studies**

The *in vivo* floating behavior can be investigated by x-ray photography of hollow microparticulate loaded with barium sulphate in the stomach of beagle dogs. The *in vivo* plasma profile can be obtained by performing the study in suitable animal models. [57]

Application of Multiparticulate Gastro-Retentive Drug Delivery System

Gastro-retentive multiparticulate drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability. These are summarized as follows.

Sustained Drug Delivery

Hollow microspheres of non-steroidal anti inflammatory drugs are very effective for controlled release as well as it reduces the major side effect of gastric irritation; for example floating microspheres of indomethacin are quiet beneficial for rheumatic patients.[58]

Site-Specific Drug Delivery

These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, e.g., Riboflavin, furosemide. Bilayer-floating capsule was developed for local delivery of misoprostol, which is a synthetic analogue of prostaglandin E1 used as a protectant of gastric ulcers caused by administration of NSAIDs. [59]

Absorption Enhancement

Drugs that have poor bioavailability because of site specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption. [60]

Future Prospects

Floating multiparticles can greatly improve the pharmacotherapy of the stomach through local drug release, used to eradicate *helicobacter pylori* from the sub-mucosal tissue of the stomach most effectively and making it possible to treat stomach and duodenal ulcers, gastritis and oesophagitis. This system allows administration of non-systemic, controlled release antacid formulation containing calcium carbonate and also locally acting anti-ulcer drugs. In stomach buoyant microparticles are considered as a beneficial strategy for the treatment of gastric and duodenal cancers. Floating multiparticulate systems may be used as a carrier for the drugs having narrow absorption windows, for example antiviral, antifungal and antibiotic agents (sulphonamides, quinolones, penicillins, cephalosporins, aminoglycosides and tetracyclines) are absorbed only from very specific regions of GI tract. In addition, by continually supplying the drug to its most efficient site of absorption, the dosage form may allow for more effective oral use of peptide and protein drugs such as calcitonin, erythropoietin, vasopressin, insulin, low molecular weight heparin. Floating microparticles of NSAIDs are very effective for reducing their major side effect, gastric irritation as well as for controlled release.

CONCLUSION

Gastro retentive multiparticulate have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs. Multiparticulate drug delivery systems provide several all the advantages including greater flexibility and adaptability of microparticulate dosage forms which gives clinicians and those engaged in product development powerful new tools to optimize therapy. The increasing sophistication of delivery technology will ensure the development of increasing number of gastro-retentive drug delivery systems to optimize the delivery of molecules that exhibit narrow absorption window, low bioavailability and extensive first pass metabolism. The control of gastro intestinal transit could be the focus of the next decade and may result in new therapeutic possibilities with substantial benefits for patient.

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