International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1510-1520 www.ijprajournal.com ISSN: 2456-4494

Gastroretentive Floating Beads – An Emerging Trend In Drug Delivery

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Submitted: 10-04-2022 Accepted: 28-04-2022

Inrecent years, novel drug delivery system has gained immense attention in pharmaceutical Industry and Academics. Scientific and technological breakthroughs in the research and development of rate-controlled oral drug delivery systems have been made by overcoming physiological challenges such as short gastric residence times and unpredictable gastric emptying times.Gastro retentive drug delivery system has gained a significant popularity in oral drug delivery. The main goal of any drug delivery system is to bring the desired concentration of drug into the blood or tissue, which is clinically effective and non-toxic over a prolonged period.This aids in improved absorption for drugs with a narrow absorption window and drugs that have pH dependent solubility.The purpose of this study is to compile the recent advances in Gastro retentive floating delivery system in particular and provide an insight into its advantages over single unit dosage form.

Keywords: floating system, oil entrapped floating beads, gastroretentive drug delivery system

I. INTRODUCTION:

Oral administration of drugs is one of the preferred routes and widely used formulations for existing and new drugs because of its flexibility in formulation, storage, and patient compliance. Despite being a dominant approach, oral drug delivery systems face challenges such as low bioavailability due to gastrointestinal system heterogeneity, pH of commensal flora, retention time of dosage form in gastric region, surface morphology and metabolic activity.

Several technological attempts have been made in the development of rate-controlled oral medication delivery systems, with the failure of conventional drug delivery systems to retain drugs in the stomach potentially leading to the development of GRDDS.[1]Gastro retentive drug delivery system are dosage form that can be retained in the stomach, delivering the drug at a steady state in a controlled and reproducible manner minimizing fluctuations in plasma concentration. [2]

GRDDSs can improve the controlled delivery of drugs with an absorption window by continuously delivering the drug for a long time before it reaches its absorption site. Prolonged gastric retention improves bioavailability, tends to reduce drug waste, and enhances solubility for drugs that are less soluble in high pH environments.It can also be used to target the drugs to a specific site in the stomach and proximal small intestine to provide local and systemic effects. Gastro retention aids in the elevated advent of new products with novel therapeutic value and significant patient benefits. [3]

The controlled gastric retention of solid dosage forms may be achieved by gastro retentive technologies including floating systems,swellable and expandable systems,high-density systems,bioadhesive systems,altered shape systems,gel-forming solution or suspension systemsand sachet systems.[4]

GASTRIC EMPYING

The ability to prolong and control the emptying time of drug formulations, which reside in the stomach for a longer period of time than conventional dosage forms, is a valuable asset.There are several challenges in designing sustained release systems for improved absorption and bioavailability. [5]The residence time is an essential factor in limiting oral bioavailability in the stomach and upper intestine. It also altered the in vitro and in vivo release profiles of the conventional oral dosage form. Sustained drug delivery systems with a longer residence time in the stomach can be used to overcome this restriction and significantly improve the solubility and dissolution rate of these drugs thereby improving bioavailability[6].

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INFLUENTIAL FACTORS ON GASTRIC RETENTION:

Several factors affect the gastric residence time of the oral dosage form such as the size, pH, viscosity and biological factors (age, disease state, stress conditions). [7]

Particle size and shape:

The particle size should be between 1 and 2 mm in order to pass through the pyloric valve and into the small intestine. According to studies, the size of a dosage form can influence its gastric emptying in the fed state. [8]Small-size tablets pass through the stomach during the digestive phase, whereas large-size tablets pass through during the housekeeping waves. Dosage forms with a diameter greater than 7.5 mm get a longer gastric residence time than one with a diameter of 9.9 mm.

According to a study conducted by Garg and Sharma, tetrahedron and ring-shaped devices have a shortened gastric residence time than other patterns.[9] The diameter of the dosage is also an important formulation parameter.

Density:

The density of a dosage form also controls the degree of gastric emptying. A buoyant dosage form floats since its density is less than that of the gastric fluids. The density is ought to be less than that of gastric contents (1.004gm/ml). To demonstrate floating property, a density of less than 1.0 gm/cm ^{3} is required.[10]As the dosage form is located away from the pylorus, the dosage unit is retained in the stomach for an extended period of time.

Gastrointestinal pH:

The pH of the abdomen is 1.5 to 2.0 when fasting, and 2.0 to 6.0 when fed. A large amount of water administered orally raises the pH of gastric acid from 6.0 to 9.0. Because the stomach does not have time to produce enough acid when the liquid empties the stomach, basic drugs have a better chance of hydrolysing in a fed state than in a fasting state. [11]

Caloriccontent:

The rate of gastric emptying is determined primarily by the viscosity, volume, and caloric con tent of the meal. The nutritive density of meals imp acts gastric emptying time.

It makes no difference whether the meal contains a lot of protein, fat, or carbohydrates as long as the ca loric content is the same. An increase in acidity and caloric value, on the other hand, slows down gastri c emptying time. [12]

GASTRORETENTIVE FLOATING SYSTEM:

Floating (FDDS) or hydrodynamic drug delivery systems or allied Balanced Systems (HBS), which was first described by Davis in 1968 are low-density systems that are gaining popularity due to their broad applicability in drug targeting to the stomach.

The floating system has sufficient buoyancy to float above the stomach contents and remain floating in the stomach without affecting the rate of gastric emptying for a prolonged period of time. While the system floats on the stomach content, the drug is released slowly at the desired speed of the system. After the drug is administered, the stomach's residual system is emptied. As a result, the gastric retention time (GRT) is increased, and the fluctuation in plasma drug concentration is controlled. [3]

Floating drug delivery formulations and the polymeric materials used in such systems have advanced significantly, enabling them to do more than simply extend the effective release period of a specific drug. Current floating drug release systems, for example, can respond to changes in the biological environment by delivering or ceasing to deliver drugs based on these changes. Various materials, including tablets, capsules, and microparticles, have been used to develop floating drug delivery systems (FDDS), that will lead to targeted delivery systems in the stomach.[14]

The floating drug delivery system improves patient compliance by reducing dosing frequency, improves the therapeutic effect of drugs with short half-lives, improves absorption of drugs that only solubilizes in the stomach, and aids in achieving peak plasma concentration.

METHODS FOR DEVELOPMENT OF FLOATING DRUG DELIVERY:

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are Two distinct buoyancy-based technologies have been used in the developm

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ent of multiparticulate gastro retentive drug deliver y systems. [15],

1. Effervescent
2. Non-effervescent approaches.

EFFERVESCENT SYSTEM:

It is a matrix-type framework designed with swellable polymers such as methylcellulose and Chitosan, as well as other effervescent compounds. As an example, consider sodium bicarbonate, tartaric acid, and citric acid. When these come into contact with gastric content, CO2 is liberated and entrapped in swollen hydrocolloids, providing buoyancy to the dosage form and potentially creating it to float over time. An alternative is to incorporate a liquid-containing matrix component, which yield gas that evaporates at body temperature.[16]

NON EFFERVESCENT SYSTEM:

Non-effervescent FDDS based on polymer swelling mechanism or bio adhesion to mucous membrane in GIT. Non-Effervescent FDDS incorporate a high level (20–75% w/w) of one or more gel-forming, highly swellable, cellulosic hydrocolloids gel-forming (or) swellable cellulose type of hydrocolloids, which can be done by mixing the drug with gel-forming hydrocolloids that swell in contact with gastric fluid after oral administration and maintain morphology integrity and a bulk density barrier, the air trapped by swollen polymer results in buoyant force to the dosage forms.[17]

GASTRO RETENTIVE FLOATING BEADS:

Floating beads are multi-unit dosage forms that achieve the goal of developing a gastro retentive drug delivery system is to maintain the drug's release action, as well as to improve the therapeutic effect of the dosage form in the stomach or gastric media until all of the drugs are completely released in the desired period. Floating beads can be prepared using polymers such as alginates, polycarbonate/dichloromethane, CAB/Eudragit RL100 mixture in acetone, and Eudragit S100/isopropanol.[18]

The floating beads are made by solvent evaporation, or by incorporating a gas-forming agent such as $CaCO_3$ or a porous structural element. [19]

A few of the strategies and materials that have been reported are Hydrogel hydrocolloids with light mineral oils, a mixture of sodium alginate and sodium bicarbonate and multi-unit floating pills that generate carbon dioxide when ingested,floating mini capsules with a core of sodium bicarbonate, lactose and PVP coated with HPMC and floating systems based on ion exchange resin technology. [20]

HYDROCOLLOIDS USED IN FLOATING BEADS:

ALGINATE SALTS:

Naturally occurring polysaccharides sodium alginate has received much attention in drug delivery systems for their excellent biocompatibility Alginate is a naturally occurring linear anionic heteropolysaccharide isolated from bacteria and brown seaweed and marine algae.Laminaria hyperborea, Ascophyllum nodosumand Macrocystis pyrifera are used to produce commercial alginates.

This material is characterized by its relatively low cost, low toxicity, biocompatibility, and biodegradability and consists of (1, 4) linked -D-mannuronate (M) and its C-5 epimer -L-guluronate (G) residues. Alginates are used as gel-forming or matrix-forming hydrocolloids in the development of beads. The ionotropic gelation method is employed for the development of Alginate beads. Beads that are approximately 2.5 mm in diameter can be prepared by dropping a sodium alginate solution into aqueous solutions of calcium chloride, causing precipitation of calcium alginate. [21] The beads are then snapped apart and frozen in liquid nitrogen before being freeze-dried at −40°C for 24 hours, resulting in the formation of a porous system that can maintain a floating force for 12 hours.

The beads are prepared in a cross-linking solution containing calcium chloride and acetic acid in a specific amount. The entrapment efficiency of alginate gel beads with a low concentration of calcium chloride was greater than that with a higher one. A high concentration of calcium chloride also provides a slow release rate. The variation in alginate concentrations had no effect on the entrapment. The release rate and weight of beads increase with an increase in sodium alginate concentration. [22]

Gadad et al. prepared sodium alginate floating beads containing cefpodoxime proxetil, a third-generation cephalosporin antibiotic by precipitation method using calcium carbonate as gas generating agent, which forms pores. The size of the beads was in the range of 700-1000 µm which can be increased as an increase in the concentration of the gas-forming agent and decreases with an increase

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Volume 7, Issue 2 Mar-Apr 2022, pp: 1510-1520 www.ijprajournal.com ISSN: 2456-4494

in the concentration of sodium alginate.The porosity of the material is based on the concentration of the gas-forming agent. All the formulations showed good floating time. The in vitro dissolution study reveals that the concentration of the gas generating agent and sodium alginate affects the release rate. [23]

PECTIN:

Pectin is a structural anionic complex polysaccharide found in terrestrial plants cell walls. Structurally, pectin consists mainly of D-galacturonic acid (GalA) units joined in chains by (1, 4) glycosidic linkages.[24]

Pectin's tendency to form gels is its most distinctive feature. This is the characteristic that makes it a valuable ingredient in a broad range of food and pharmaceutical products. The degree of esterification (DE) of the carboxylic groups to methyl ester groups tends to affect this property.In the presence of calcium ions, pectin polymerizes in either cold or hot water, increasing viscosity and accelerating gelation. [25]The degree of gelation depends upon the concentration of pectin used.The concentration range used for most applications is between 0.15and 3.1percent.

Badve et al. Diclofenac sodium hollow calcium pectinate beads were developed for their chronopharmacological ability. The floating beads were structurally hollow bodies with an apparent density of less than 1 g/mL and a porosity of 34%[26].

Another study, reported floating cinnarizine gel calcium pectinate beads were prepared. In healthy human volunteers, the studies discovered improved in vivo efficacy of up to 3.80 times when compared to conventional tablets. Beads made of LM-pectin (base), glyceryl monooleate (GMO), and labrafac lipophile WL 1349 (oil phase) had instant in vitro floating potential, excellent floating properties, high loading efficiency, and zero-order release patterns.[27] These properties suggest that they could be used for once-daily cinnarizine administration.

CASEIN:

Casein-like, albumin, and gelatin a lyophilic colloid in nature. Casein is a mixture of phosphor proteins of differing molecular weight. Casein is a major milk protein and has an isoelectric point at pH 4.6.[28] Caseinates readily form a gel when slowly coagulated from concentrated solutions. Casein-based microparticles entrapping bioactive molecules were prepared via emulsification-chemical crosslinking with glutaraldehyde, enzymatic crosslinking by transglutaminase, simple conservation, and electrostatic complexation. [29]

Bulgarelli et al. The effect of matrix composition and process conditions on casein gelatin beads prepared using the emulsification extraction method were investigated.The emulsification method was used to generate casein-gelatin beads.The emulsifying properties of casein cause the incorporation of air pockets and the formation of large cavities in the beads.The matrix's high porosity influences bead characteristics such as drug content, dissolution rate, and floatation. [30]

GELUCIRES:

Glaciers are glycerides and polyglycolide of fatty acids of vegetable origin. [31] Gelucire is inert, semisolid, waxy excipients that are surface-active in nature and form micelles, microscopic globules, or vesicles when dispersed in aqueous media. The polymer is composed of a mixture of mono-, di, and triglycerides and mono- and di- fatty acid esters of polyethylene glycols. The lipidic nature of gelucire makes it highly biocompatible and biodegradable.[32] Gelucire-based emulsion gel beads are explored for their potential to prevent gastric irritation of drugs by forming a protective coat around them.

Shashank Soni et al. conducted a study to investigate the feasibility of Gelucire-based floating emulsion gel beads as a sustained stomach-specific drug delivery carrier for model drugs metronidazole (MTZ) or norfloxacin (NFC). Emulsion gel beads were prepared by extruding Gelucire (39/01 + 50/13) - sodium alginate emulsions loaded with model drugs (metronidazole or norfloxacin) and buoyancy imparting agent (CaCO3) into warm acidic CaCl2 solution (3% w/v, 37ºC). Prepared beads showed high drug encapsulation efficiency; excellent buoyancy and released the model drugs MTZ and NFC in a sustained manner in 0.1 M HCl over an extended period of time.[33]

CHITOSAN:

Chitosan is a hydrogel, natural linear biop olyaminosaccharide acquired by alkalinedeacetylati on of chitin.[34]Chitin is a straight homopolymer composed of - (1, 4)-linked N-acetyl-glucosamine units, while chitosan comprises of copolymers of glucosamine and N-acetyl-glucosamine. The emulsion cross-linking and the inotropic gelation

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1510-1520 www.ijprajournal.com ISSN: 2456-4494

are most preferred and widely used methods for the preparation of floating microspheres. Due to the incredible ionic nature of both methods, cross-linking is considered necessary. Different grades of chitosan are available due to high degree of deacetylation and molecular weight, and their solubility fluctuates from slightly acidic to aqueous.[35]

BehinSundara Raj et alformulated and evaluated chitosan Prazosin beads by Ionotropic gelation method. Prazosin loaded chitosan polyelectrolyte complex (PEC) hydrogel beads were prepared via ionotropic gelation and ionotropic crosslinking with sodium tri-polyphosphate (TPP). To achieve spherical beads, the prepared beads were explored for optimal stirring conditions and curing periods. Over a 7-hour study period, the in-vitro dissolution rate profile revealed a sustained release of the drug from the beads. Prazosin release decreased as chitosan concentration increased.[36]

GASTRO RETENTIVEOIL ENTRAPPED FLOATING BEADS:

Oil entrapped Floating beads are Non-effervescent floating dosage forms that use low-density substances such as polymers that swell or gel in the acidic medium and can achieve low density by themselves or by entrapping other low-density excipients like oils and fatty substances.[37] The use of oils not only diminishes their density enough to float over stomach contents but also tends to slow polymer hydration and prevent faster erosion.

The formulations made using hydrocolloids, polysaccharides, and gel-forming polymers are usually a simple blend of the drug and polymer thoroughly mixed with other manufacturing aids and made into a capsule. Following oral administration, the dosage form swells and gels in contact with gastric fluids, attaining a bulk density lower than the gastric fluid, enabling it to float. The air entrapped within the swollen gel matrix imparts buoyancy to the dosage forms. The gel layer that forms also acts as a barrier to the entry of gastric medium into the system and the concurrent drug transport out of the system.As a result, the drug is released in a sustained manner over time. In many cases, polymers are either used singly or in combination with others mainly to modulate the swelling and erosion behaviour of the matrix and to achieve the desired drug-release pattern.[38]

PREPARATION OF OIL ENTRAPPED BEADS:

IONIC GELATION METHOD:

Ionic gelation is a chemical reaction that occurs between polymer and cross-linker like calcium chloride in which the polymer ions are replaced by calcium ions to form a structure resembling a gel. Beads prepared by ionotropic gelation are due to the ability of polyelectrolytes to crosslink with counter-ions to initiate cross-linking. The calcium ion in the solution minimizes the electrostatic repulsion between the functional groups in the polymer strands and results in a calcium-polymer gel meshwork structure. Once gelation is complete the formed beads are separated from the solution and dried. The concentration of polymer and drop volume are critical factors adjusted to obtain spherical beads ranging in size from 1-2 mm in diameter.[39]

The mechanism of crosslinking polymer (Ionic gelation) can be accomplished by two sub-methods, external or internal gelation method. [40]The methods differ from each other in the source of the crosslinking ion.

External gelation or diffusion method:

In the External gelation method the cross-linker, acting as cations, diffuses from the external medium into the interior of the polymer network to form the hydrogel beads. The active compound to be encapsulated is stirred with the polymer solution to achieve the desired concentration, and then the solution is drawn into a syringe with a 26 G needle and extruded manually drop wise into an aqueous solution containing cross-linking cations (calcium chloride solution) as soon as the polymer drop comes in contact with the cross-linker instant gelation occurs. The formed beads are filtered using a strainer, rinsed using distilled water, and stored under refrigeration.

Internal gelation or emulsification method:

As an alternative to external gelation, emulsification/internal gelation has been proposed. The method is proposed for producing small diameter beads in large quantities.

The polymeric beads are formed through the internal gelation of polymer and cross-linker cations. For internal gelation, the cations are released from the interior of the polymer phase to form the hydrogel beads. The active compound is mixed with the cross-linker solution and dropped into a polymer solution using a syringe; the cation is released by acidification of the medium, and the formed beads are separated and stored.

POLYELECTROLYTE COMPLEXATION METHOD:

Polyelectrolyte complexion tools for bead development are based on the complexation of

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1510-1520 www.ijprajournal.com ISSN: 2456-4494

polymeric materials with opposite charges.[41] The technique involves the addition of one polyelectrolyte to another polyelectrolyte having an opposite charge leading to complex coacervation of polyelectrolytes, polycation, and polyanion materials. Upon gelation, the mixture will separate into a dense coacertive phase containing the microbeads and a dilute equilibrium phase. The prepared beads remained stable over a large range of pH.

EMULSION GELATION METHOD:

Emulsion gelation techniques are yet another process of preparing beads. The polymer solution was prepared by dispersing the weighed quantity of polymer in deionized water. Further, the drug is dissolved or dispersed in the polymer solution yielding a homogenous drug-polymer mixture. A sufficient amount of cross-linking agent is required to create a viscous dispersion, which is then extruded through a syringe with a flat-tipped syringe of size 23 into an organic phase with a span of 80 while magnetic stirring is kept at 1500 pm. The formed beads are retained in the oil for 30 min to produce rigid discrete particles. Further collected by decantation and the products thus separated were washed with chloroform to remove the traces of oil, dried at 400ºC for 12 h.[42]

DEVELOPMENTS INOIL ENTRAPPED FLOATING ALGINATE BEADS:

Alginate beads are formulated from free dried calcium alginate by solubilizing sodium alginate solution in cross linker such as aqueous calcium chloride. Water phase is emulsified with addition of oil to form an emulsion. [43]Drop-wise inclusion of sodium alginate to calcium chloride solution results in instant gelation of the droplet surface attributed to the formation of calcium alginate. Several studies investigated the incorporation of oil entrapped into beads and their efficiency.

Murata et al.developed calcium-induced alginate floating beads of metronidazole for treatment of H. pylori using two techniques. At room temperature, a solution containing sodium alginate, drug, and vegetable oil is dropped into a 0.1M calcium pantothenate solution.Instantaneous gelation on the outer surface of the droplets occurred as insoluble calcium alginate beads were formed. The resultant hydrogel beads were washed twice and used for in vitro evaluation. It was observed during in vitro studies that beads with a vegetable oil content of 30% w/w did not sink and remained buoyant due to entrapment of low-density vegetable oil in the alginate gel matrix, whereas beads prepared without any oil settled at the bottom of the vessel and beads with 10% to 20% w/w oil content initially sank however, it gradually floated due to the continuous release of metronidazole. Beads with all levels of added vegetable oil had a higher metronidazole loading capacity than calcium alginate beads alone.[44]

Using the same method, alginate beads containing chitosan were prepared. The air trapped during the formation of chitosan-based alginate beads provided buoyancy, enabling them to float over the dissolution medium.[45] Chitosan content amounting to 5% w/w was found to be necessary to allow the beads to remain buoyant, but its molecular weight or deacetylation ratio did not affect buoyancy. Floating was not recorded when polymers apart from chitosan were used, such as chitin, curdlan, sodium dextran sulphate, and xylan.The drug loading efficiency of beads (65%) reported using this method was not promising. Because of the high porosity origin of the chitosan utilized, metronidazole release from chitosan-based alginate beads was found to be faster in vitro.

Inderbir Singh et al. formulated and evaluated Domperidone loaded mineral Oil entrapped emulsion gel buoyant bead by Emulsion gelation technique. The particle size, surface morphology, buoyancy, actual drug content, and entrapment efficiency of the prepared beads were all evaluated. The impact of various oils (castor oil, olive oil, and linseed oil) as well as oil concentration levels (10%, 15%, and 20% w/w) on the uniformity, homogeneity, and integrity of the beads was also studied.In-vitro drug release results showed that linseed oil was a better release retardant than castor oil and olive oil. Furthermore, the beads formulated with 15% w/w linseed oil had a more uniform shape, maximum buoyancy, and minimal oil leakage.[46]

Rammohan Bera et al. formulated and evaluated (in-vitro) of Sunflower Oil Entrapped within Buoyant Beads of Furosemide. The emulsion-gelation technique was used to develop buoyant alginate beads of furosemide entrapped in sunflower oil. During the preparation of different batches of beads, the ratios of sunflower oil to water (v/v) and drug to polymer (w/w) were kept as variables at two levels: high or low. Smooth, spherical beads with a nominal weight variation were produced. With a lag time of 5 minutes, all batches of beads floated for 24 hours. The release of the drug followed for5 hours. Higuchi and first-

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 1510-1520 www.ijprajournal.com ISSN: 2456-4494

order kinetic modelling indicated a diffusion-controlled release of drugs from the beads. The study also demonstrated the influence of sunflower oil on drug entrapment (81–95%) and in-vitro release. When compared to a lower level of oil-containing beads, a higher level of oil increased drug entrapment efficiency but slowed the drug release rate.[47]

APPLICATION:

Gastro retentive floating beads have a number of applications for drugs with low bioavailability due to the narrow absorption window in the upper gastrointestinal tract. The system keeps the dosage form at the site of absorption, increasing bioavailability. [48]

Site-Specific Drug Delivery

These systems are especially useful for drugs that are absorbed specifically from the stomach or the proximal part of the small intestine, including riboflavin and furosemide. Furosemide is absorbed predominantly through the stomach, followed by the duodenum. Previous studies reported that a monolithic floating dosage form with a prolonged gastric residence time was developed, which resulted in increased bioavailability. The AUC of the floating tablets was higher than that obtained from conventional furosemide tablets. [49]

Absorption Enhancement:

Drugs with poor bioavailability owing to site-specific absorption from the upper gastrointestinal tract are attractive targets for formulation as floating drug delivery systems, achieving absorption. E.g. A significant increase in the bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%) and enteric-coated LASIX-long products (29.5%).

Diminished adverse effects in the colon:

The drug in the Floating drug delivery system is retained in the stomach, restricting the amount of drug that enters the colon. As a result, undesirable drug activity in the colon can be avoided. The incorporation of oil provides buoyancy to beads thereby aiding in gastro retention for drugs sensitive to the colon region. [50]

Reduced fluctuations of drug concentration:

In contrast to immediate release dosage forms, continuous drug input after CRGRDF administration results in blood drug levels within a narrower range. As a consequence, fluctuations in drug effects are limited, and concentration-dependent adverse effects associated with peak concentrations can be avoided. This property is especially important for drugs with a potential therapeutic index.

MARKETED PRODUCT OF FDDS:[51]

S.NO	BRAND NAME	ACTIVE INGREDIENT	TECHNOLOGY
1.	Topalcan	Al-Ag antacid	Floating liquid alginate
2.	Medopar	Levodopa and Bensarazide	Floatingcapsules (Controlled release)
3.	Cytotec	Misoprosol	Bilayer floating capsules
4.	Cifran OD	Ciprofloxacin	Gas generating floating system
5.	Zanocin OD	Ofloxacin	Effervescent Floating system
6.	Baclofen GRS	Baclofen	Floating and Swelling system
7.	Liquid Gaviscon	Aluminium hydroxide and Magnesium carbonate	Effervescent Floating liquid alginate, Raft forming system
8.	Coreg CR	Carvedilol	Gastro retention system

FUTURE SCOPE OF FLOATING MULTIPLE UNIT DRUG DELIVERY SYSTEM

Gastro retentive beads contribute to higher permeation of medications absorbed from the top section of the stomach, resulting in increased bioavailability and regulated distribution of a wide range of pharmaceuticals, providing innovative and significant treatment options.[52]Future studies should focus on a few of the following areas:

Development of single-step and easily scalable production techniques. Because most of the currently available techniques appear to be complex, necessitating the use of a large number of excipients and involving multiple-step process

International Journal of Pharmaceutical Research and Applications
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using organic solvents, they have limited applicability for industrial-scale production. Design of multifunctional excipients that allow for the use of low levels of polymers in the dosage form and increase the drug-loading efficiency.Development of new formulation techniques to provide dosage forms that can sustain floating after a succession of meals and provide meal-independent gastric retention properties suitable for administration to patients with a wide range of eating habits.

Establishment of a correlation between prolonged gastric retention and pharmacokinetic characteristics of a dosage form using more sophisticated in vivo imaging techniques.Investigation of the effects of posture on the performance of single- compared with multi-unit floating dosage forms when taken before or after a meal.Applicability of a combination of two or more mechanisms of gastric retention (e.g., floating and mucoadhesion) to provide site-specific delivery and reproducible GRTs.

INNOVATIVE TECHNOLOGIES IN GASTRO RETENTIVE FLOATING SYSTEM:

1. Gastro Retentive Innovative Device (GRID)

The Gastro Retentive Innovative Device is an effective once-daily method for medications that would otherwise be absorbed only in the stomach or small intestine. GRID is intended to keep medicines in the stomach for 6 to 8 hours. Drug absorption is increased when drugs are kept in the stomach for a longer period of time. This revolutionary technology combines several advanced coatings. It floats directly on the gastric contents during the absorption of the dosage type in conjunction with food. GRID coatings are activated by gastrointestinal fluid, which gradually causes swelling up to an initial volume of eight to eleven times. As a result, plasma concentrations of drugs are maintained in the therapeutic range for a longer period of time; thus, this dosage type can be used as a "once-a-day" device.[53]

2. IPDAS® Technology (Intestinal Protective Drug Absorption System)

IPDAS is a multiparticulate-based extruded and spheronised technology. In this technique beads containing a high-density drug are compressed to form controlled-release tablets through this technique. It is especially useful for tablets that cause gastro irritation and disintegrate quickly.[54] The origin of the drug-containing bead matrix or its semi-permeable membrane coating controls the release. It was initially developed for a proprietary formulation of naproxen with a fast onset of action to relieve pain over a 24-hour period, which is marketed in the United States and Canada as Naprelan.

3. CODAS® technology (chronotherapeutic oral drug absorption system)

CODAS technology is intended to prolong drug release for a predestined period of time in order to tailor therapy to the body's circadian rhythms. The technology is once again based on a polymer coated Multiparticulate system. The release controlling coating is a polymer blend that is both water-soluble and water-insoluble. When water from the gastrointestinal tract comes into contact with the polymer-coated beads, the water-soluble polymer gradually dissolves, designed to allow the drug to diffuse through the resulting pores in the coating. The water-insoluble polymer continues to act as a barrier, allowing the drug to be released at a predictable rate.[55]

4. Diffucaps®

A System for Multi particulates Customized drug release features are derived using Errand's Diffucaps® multiparticulate system by first layering therapeutic agent onto an inert core (such as a sugar/cellulose sphere), then incorporating one or more rate-controlling, functional polymers to generate spherical, multi-layered particles. [56]The Innopran® XL tablet from Eurand is a commercialized product of the Diffucap® multiparticulate system.

5. Acuform® technology

Acuform® a proprietary formulation of Depomed, is a polymer-based technology designed to improve GIT drug delivery. This technology enables targeted and controlled drug delivery to the proximal (upper GIT), which is the preferred absorption site for many oral drugs. This technology is an efficient drug delivery method, particularly for drugs absorbed in the upper GI tract. It is also useful for drugs that are insoluble in water, irritate, or are unsafe for the small intestinal mucosa in the distal GIT region, and it is more efficient when drug plasma levels fluctuation is less.[57]

6. Oleotec™ and Soctec™

OleotecTM and SoctecTM are gastrointestinal-retentive capsule technology innovated by Skyepharma. The Oleotac TM technique is designed for drugs with high therapeutic doses, but it is not ideal for traditional dosage methods. This method yields drugs that have an effect primarily in the proximal

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Volume 7, Issue 2 Mar-Apr 2022, pp: 1510-1520 www.ijprajournal.com ISSN: 2456-4494

gastrointestinal tract. The Oleotec method is essentially a gel that is incorporated in the form of a stick pack and forms a continuous coating on the stomach walls.[58]The Soctec TM system is designed for medicines to be administered as a controlled release and absorbed in the proximal part of the intestine in order to improve drug bioavailability. Soctec is an elongated capsule containing a drug. It can be used to offer a wide range of medications.[59]

II. CONCLUSION:

Floating multi-particles can greatly improve the pharmacotherapy of many drugs, despite extensive research in the area of GRDDS success has been very limited, with only a few drug products reaching the market. Drug absorption in the gastrointestinal tract is a wildly varying systematic process, and prolonging gastric retention of the dosage form improves drug absorption time. These of the stomach, enhance the bioavailability and controlled delivery of many drugs with new and vital therapeutic options. This leads to less frequent dosing and more advantageous efficiency of the treatment. Good stability and better drug release as compared to other conventional dosage forms make such a system greater reliable.Gastro retentive systems offer the gain of better absorption of medication that is absorbed from the upper GIT and apparently a large number of formulations have shown successfully in vitro performance. Floating drug delivery systems are expected towards becoming progressively more important, ultimately leading to improved efficiencies of various types of therapeutic interventions. Despite the fact that there are a number of challenges to overcome in order to achieve prolonged gastric retention, a large number of companies are focusing on pursuing and commercializing this technique.

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