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FLOATING MICROSPHERES AS GASTRORETENTIVE DRUG DELIVERY SYSTEMS: A REVIEW

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ABSTRACT

Among the different routes of drug administration, the oral route has achieved the most attention among the researchers. Microspheres constitute an important part of these particulate drug delivery systems by virtue of their small size and efficient carrier characteristics. Gastro retentive multiparticulates have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs. Floating microspheres have been gaining importance due to the uniform distribution of these multiple-unit dosage forms in the stomach, which results in more reproducible drug absorption and reduced risk of local irritation. Such systems have more advantages over the single-unit dosage forms. The present review briefly addresses the physiology of the gastrointestinal tract and the factors affecting the gastric retention time. The purpose of this review is to bring together the recent literature with respect to the approaches to achieve gastric retention, classification and characterization of floating drug delivery system, their advantages and limitations.

KEYWORDS: Microspheres, Gastro retention, Floating microspheres, Drug delivery system.

INTRODUCTION

Drug delivery technology is one of the frontier areas of research in the field of science and technology. Considerable attention is focused on the development of controlled drug delivery systems offering the advantages of better therapeutic efficacy and easier to comply with than

the conventional regimens requiring more frequent dosing.[1] The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration. Controlled release (CR) systems provide a uniform concentration/ amount of drug at the absorption site, and thus, after absorption, allow maintenance of plasma concentrations within a therapeutic range, which minimizes side effects and also reduces the frequency of administration. CR products are formulations that release active drug compounds into the body gradually and predictably over a 12 to 24 hour period and that can be taken once or twice a day. Typically, these products provide numerous benefits compared with immediate release drugs including greater effectiveness in treating chronic conditions, reduced side effects, greater convenience and higher levels of patient compliance due to a simplified dosing schedule. Because of the above advantages, such systems form the major segment of the drug delivery market.[2]

The oral route is considered as the most promising route of drug delivery. Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range needed for treatment, only when taken several times a day. This results in significant fluctuation in drug levels. Recently, several technical advancements have led to the development of several novel drug delivery systems (NDDS) that could revolutionize the method of medication and provide a number of therapeutic benefits.[3]

Microparticles are defined as spherical polymeric particles with sizes ranging from 1 to 1000 μm. There are two subtypes of microparticles. Microcapsules are vesicular systems in which the drug molecules are surrounded by a membrane. Microspheres are matrix systems in which the drug molecules are dispersed throughout the particle. Microspheres constitute an important part of these particulate drug delivery systems by virtue of their small size and efficient carrier characteristics.[4]

GASTRORETENTIVE DRUG DELIVERY SYSTEMS (GDDS)

The oral route is considered as the most promising route of drug delivery. Effective oral drug delivery may depend upon the factors such as gastric emptying process, gastrointestinal transit time of dosage form, drug release from the dosage form and site of absorption of drugs. Most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, because of variable gastric emptying leading to non-uniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach. This leads to incomplete absorption of drugs having absorption window

especially in the upper part of the small intestine, as once the drug passes down the absorption site, the remaining quantity goes unabsorbed.[5]

Basic Gastrointestinal tract physiology

Anatomically, the stomach is divided into 3 regions: fundus, body, and antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions.[6]

It has been reported that the mean value of pH in fasted healthy subjects is 1.1± 0.15. But when food comes into the stomach, the pH may rise to levels in the 3.0 to 4.0 level due to the buffering capacity of proteins. However, in fasted state, basal gastric secretion in women is slightly lower than that of men.[7]

Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the two states. During the fasting state an interdigestive series of electrical events takes place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 phases:[8]

1. Phase I (Basal Phase) lasts from 30 to 60 minutes with rare contractions.
2. Phase II (Preburst Phase) lasts for 20 to 40 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (Burst Phase) lasts for 10 to 20 minutes. It includes intense and regular contractions for short period.it is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.
4. Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

After the ingestion of a mixed meal, the pattern of contractions changes from fasted to that of fed state. This is known as digestive motility pattern and comprises of continuous contractions as in Phase II of fasted state. These contractions result in reducing the size of food particles (to less than 1 mm), which are propelled towards the pylorus in a suspension form. During the fed state onset of MMC is delayed resulting in slowdown of gastric

emptying rate. Scintigraphic studies determining gastric emptying rates revealed that orally administered controlled release dosage forms are subjected to basically 2 complications, that of short gastric residence time and unpredictable gastric emptying rate.[9]

Potential Drug Candidates for Gastroretentive Drug Delivery Systems

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

Drugs those are unsuitable for Gastroretentive Drug Delivery Systems

1. Drugs that have very limited acid solubility eg. Phenytoin, etc.
2. Drugs that suffer instability in the gastric environment eg. Erythromycin, etc.
3. Drugs intended for selective release in the colon eg. 5-aminosalicylic acid and corticosteroids, etc.[10]

FACTORS AFFECTING THE GASTRIC RESIDENCE TIME

The most important parameters controlling the gastric retention time (GRT) of oral dosage forms include:[6,7,10]

1. Density of dosage form: The density of gastric fluid is reported to be 1.004 gm/ml. The density of the dosage form should be less than this for buoyancy, so that it is retained in the stomach for a longer time. A density of < 1.0 gm/ cm^3 is required to exhibit floating property.[11]

2. Composition of meal: Fats, particularly fatty acids inhibit gastric secretion and have a pronounced reductive effect on the rate of emptying. Protein and starch are shown to have inhibitory effect on gastric emptying, though to a less extent. As the viscosity of the gastric fluids is increased, there is a corresponding decrease in the rate of emptying.

3. Caloric content: The gastric residence time can be increased by 4-10 hrs with a meal that is rich in proteins and fats.

4. Frequency of the food: The gastric residence time can increase by >6 hrs when successive meals are given, compared with a single meal.

5. Size of dosage form: In general larger the dosage form the greater will be the gastric retention time (GRT) as the large size of the dosage form does not allow it to quickly pass through the pyloric antrum into the intestine. This emphasizes the need for size enlargement of dosage forms in the stomach in order to prolong the gastric residence time.

6. Sex: Generally females have a slower gastric emptying rate (4.6±1.2 hrs) than males (3.4±0.6 hr) regardless of weight, height and body surface area.

7. Body posture: Gastric emptying is favored while standing and by lying on the right side since the normal curvature of the stomach provides a downhill path whereas lying on the left side retards it.

8. Emotional state of subject: The influence of emotional factors on gastric motility and secretion may be either augmentative or inhibitory depending upon whether the emotional experience is of an aggressive or a depressive type.

9. Effect of drugs: Drugs that retard gastric emptying includes poorly soluble antacids (Aluminum hydroxide), anticholinergics (Atropine, Propantheline), narcotic analgesics (Morphine) and tricyclic antidepressants (Imipramine, amitryptiline) whereas Metoclopramide, domperidom and cisapride (Ant emetics) stimulates gastric emptying.

10. Exercise: Vigorous physical activity retards gastric emptying.

11. Diseased states: Diseases like gastroenteritis, gastric ulcer, pyloric stenosis, diabetes and hypothyroidism retard gastric emptying. Partial or total gastrectomy, duodenal ulcer and hyperthyroidism promote gastric emptying rate.

12. Gastrointestinal pH: Gastric emptying is retarded at low stomach pH and promoted at higher or alkaline pH. Chemicals that affect gastrointestinal pH also alter gastric emptying. The inhibitory effect of various acids on gastric emptying decreases with increase in molecular weight and is in the following order HCl>acetic>lactic>tartaric>citric. With alkaline solutions, a low base concentration (1% NaHCO3) increases the gastric emptying rate more than the 1 of higher concentration (5%).

APPROACHES TO ACHIEVE GASTRIC RETENTION[12]

Gastroretentive drug delivery is an approach to prolong the gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastroretentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs.[10] Over the last few decades, the pursuit and exploitation of devices designed to retain drug in the upper part of GI tract has advanced in terms of technology and diversity, encompassing a variety of systems such as floating systems, raft systems, swellable systems, expandable systems, bouyant systems and low-density systems.[13] Gastroretention provides advantages in delivery of drugs with narrow therapeutic window in the small intestinal region. Also longer residence time could be advantageous for local action in the upper part of the small intestine, especially for treatment of peptic ulcers.

Several techniques are reported in the literature to increase the gastric retention of drugs:

1. High density systems

These systems must have density that exceeds the density of normal stomach content (~ 1.004 gm/cm^3), are retained in the rugae of stomach and are capable of withstanding its peristaltic movements.[14] Diluents such as barium sulfate, zinc oxide, titanium oxide and iron powder are used to manufacture such high-density formulations. A density close to 2.5 gm/cm^3 seems necessary for significant prolongation of gastric residence time. The only drawback with theses systems is the technical difficulty to manufacture them with a large amount of drug and achieve the required density.[10]

2. Floating systems

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on gastric contents, the drug is slowly released at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. The inherent low density can be provided by the entrapment of air (e.g. hollow chambers) or by the incorporation of low density materials (e.g. fatty materials or oils, or foam powder). These approaches have been used for the design of floating dosage forms of single and multi-unit systems.[13,15]

3. Swelling and Expandable systems

These systems are also called as "Plug type systems" since they exhibit tendency to remain logged in the pyloric sphincters. These polymeric matrices remain in the gastric cavity for several hours even in fed state. By selection of suitable polymers which swells upon coming in contact with the gastric fluid, various controlled and sustained dosage forms can be made. The extensive swelling of these polymers is a result of the presence of physical-chemical cross links in the hydrophilic polymer network. These cross link prevents the dissolution of polymer and thus maintains the physical integrity of the dosage form. A high degree of cross linking retards the swelling ability of the system and maintains its integrity for prolonged period. On the other hand, a low degree of cross linking results in extensive swelling followed by the rapid dissolution of the polymer.[16]

4. Mucoadhesive and bioadhesive systems

Bioadhesive drug delivery systems are used to localize a delivery device within the lumen to enhance the drug absorption in a site specific manner. This approach involves the use of bioadhesive polymers, which can adhere to the epithelial surface in the stomach. Some of the commonly used excipients in these systems include carbopol, lectins, chitosan, polycarbophil, CMC and gliadin, etc.[7]

5. Incorporating delaying excipients

This approach involves feeding of digestible polymers or fatty acid salts that charges the motility pattern of the stomach to a fed state thereby decreasing the gastric emptying rate and permitting considerable prolongation of the drug release. Prolongation of the gastric residence time of drug delivery system consists of incorporating delaying excipients like triethanolamine myristate in a delivery system.[17]

FLOATING DRUG DELIVERY SYSTEM (FDDS)

Floating drug delivery systems (FDDS) are among the several approaches that have been developed in order to increase the gastric retention time of the dosage forms.[18,19] The multi unit system has been developed to identify the merit over a single unit dosage form because the single unit floating systems are more popular but have a disadvantage owing to their "all-or-nothing" emptying process leading to high variability of the gastrointestinal transit time.[20] Still the multi unit dosage forms may be better suited because they are claimed to reduce the inter subject variability in absorption and lower the probability of dose dumping. Such a dosage form can be widely distributed throughout the gastrointestinal tract (GIT), which

afforded a possibility of a longer lasting retention and more reliable release of the drug from the dosage form.[21] Table 1 represents list of drugs formulated as floating microspheres.

Floating drug delivery systems (FDDS) can be further classified on the basis of buoyancy as:

1.Single Unit Floating Dosage systems

a.Non-effervescent systems

b.Effervescent system (Gas generating systems)

2.Multiple Unit Floating Dosage systems

a.Non-effervescent systems

b.Effervescent system (Gas generating systems)

c.Hollow Microspheres

3.Raft forming systems

1. Single Unit Floating Dosage systems

a. Non-effervescent systems

This type of system swells via imbibation of gastric fluid to an extent that it prevents their exit from the stomach. These systems are also known as "plug-type systems" as described earlier. One of the methods of preparation of such system involves the mixing of drug with a gel, which swells in contact with the gastric fluid after oral administration and attains a bulk density of less than one. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so-formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass. Various polymers such as hydroxyl ethyl cellulose, hydroxyl propyl cellulose, hydroxyl propyl methyl cellulose, sodium carboxyl methyl cellulose, polycarbophils, polyacrylates, polystyrene are incorporated in high levels to tablets or capsules.[7,22]

b. Effervescent system (Gas generating systems)

These systems are prepared by utilizing swellable polymers such as hydroxyl propyl methyl cellulose and chitosan and various effervescent compounds like sodium bicarbonate, tartaric acid, and acetic acid. As such system comes in contact with the acidic gastric contents, carbon dioxide is released which gets entrapped in swollen hydrocolloids, thereby providing buoyancy to the dosage form. The optimal stoichiometric ratio of citric acid and sodium carbonate for gas generation is reported to be 0.76:1.[9]

2. Multiple Unit Floating Dosage systems

Single unit formulation suffers from drawbacks of high variability of gastrointestinal transit time because of sticking together or being obstructed in gastrointestinal tract, resulting in irritation and all-or-none gastric emptying nature. In order to overcome the above problem, multiple unit floating systems were developed. It reduces the inter-subject variability in absorption and also lowers the probability of dose dumping.[23]

a. Non-effervescent systems

Not much literature is available on non-effervescent multiple unit systems. However, few workers have reported the possibility of developing such system containing indomethacin, using chitosan as the polymeric excipient. A multiple unit HBS containing indomethacin as a model drug prepared by extrusion process is reported. A mixture of drug, chitosan and acetic acid is extruded through needle, and the extrudate is cut and dried. Chitosan hydrates and floats in the acidic media, required drug release could be obtained by modifying the drug-polymer ratio.[22]

b. Effervescent system (Gas generating systems)

A multiple unit system comprises of calcium alginate core and calcium alginate/PVA membrane, both separated by an air compartment was prepared. In presence of water, the PVA leaches out and increases the membrane permeability, maintaining the integrity of the air compartment. Increase in molecular weight and concentration of PVA, resulted in enhancement of the floating properties of the system. Freeze-drying technique is also reported for the preparation of floating calcium alginate beads. Sodium alginate solution is added drop wise into the aqueous solution of calcium chloride, causing the instant gelation of the droplet surface, due to the formation of calcium alginate. The obtained beads are freeze-dried resulting in a porous structure, which aid in floating. The authors studied the behavior of radiolabeled floating beads and compared with nonfloating beads in human volunteers using gamma scintigraphy. Prolonged gastric residence time of more than 5.5 h was observed for floating beads. The nonfloating beads had a shorter residence time with a mean onset emptying time of 1 hr.[24]

c. Hollow Microspheres

Hollow microspheres are considered as one of the most promising buoyant systems, because of the presence of central hollow space inside the microsphere. The general techniques involved in their preparation include simple solvent evaporation and solvent diffusion and

evaporation. The drug release and better flowing properties mainly depend on the type of polymer, plasticizer and the solvents employed for the preparation. Polymers such as polycarbonate, Eudragit® S and cellulose acetate were used in the preparation of hollow microspheres, and the drug release can be modulated by optimizing the polymer quantity and the polymer-plasticizer ratio.[7]

3. Raft forming systems

Here, a gel-forming solution (e.g. Sodium alginate solution containing carbonates or bicarbonates) swells and forms a viscous cohesive gel containing entrapped CO_2 bubbles on contact with gastric fluid. The raft floats because of the buoyancy created by the formation of CO_2 and acts as a barrier to prevent the reflux of gastric contents like HCl and enzymes into the oesophagus. Formulations also typically contain antacids such as aluminium hydroxide or calcium carbonate to reduce gastric acidity. Because raft forming systems produce a layer on the top of gastric fluids, they are often used for gastro-oesophageal reflux treatment.[25,26]

Table 1: List of drugs recently formulated as floating microspheres.

S. No.	Drug	Polymer	Method	Reference
1	Ritonavir	Sodium alginate, guargum	Ionic-gelation	[27]
2	Clarithromycin	HPMC-ethyl cellulose, HPMC, eudragit S-100, eudragit L-100	solvent evaporation/diffusion	[28]
3	Salbutamol sulfate	Eudragit L100	solvent evaporation	[29]
4	Esomeprazole magnesium trihydrate	Ethyl cellulose, HPMC K4M,HPMC K15M	double emulsion solvent diffusion	[30]
5	Ketoprofen	Ethyl cellulose, HPMC	emulsion solvent diffusion	[31]
6	Carvedilol phosphate	Ethyl cellulose, eudragit RS 100	emulsion solvent diffusion	[32]
7	Captopril	Ethyl cellulose, Eudragit RS-100, Eudragit RL-100	Non-aqueous solvent evaporation	[33]
8	Diclofenac sodium	Eudragit S 100	emulsion-solvent diffusion	[34]
9	Flupirtine	Ethyl cellulose, HPMC	solvent evaporation	[35]
10	Sitagliptin	HPMC, Eudragit RS100	emulsion solvent evaporation	[36]
11	Valacyclovir	Ethylcellulose	emulsification solvent evaporation	[37]
12	Famotidine	Ethylcellulose	solvent evaporation	[38]
13	Ritonavir	Sodium alginate, HPMC	Gas generation	[39]
14	Ranitidine	Ethylcellulose	Non-aqueous solvent evaporation	[40]
15	Tolperisone	Ethyl cellulose, HPMC	Non-aqueous solvent	[41]

	hydrochloride		evaporation	
16	Captopril	HPMC K4M	solvent evaporation	[42]
17	Curcumin	HPMC, ethyl cellulose, Eudragit S 100	emulsion solvent diffusion	[43]
18	Metformin HCl	Ethyl cellulose, HPMC	Non Aqueous solvent diffusion	[44]
19	Ranitidine	Sodium alginate, Guargum and Xanthan	Ionic-gelation	[45]
20	Gabapentin	Ethyl cellulose and cellulose acetate	solvent evaporation	[46]
21	Famotidine	Eudragit RL 100, cellulose acetate	emulsion solvent diffusion	[47]
22	Trimetazidin dihydrochloride	Chitosan	capillary extrusion	[48]
23	Levofloxacin	HPMC, Eudragit S 100	emulsion solvent evaporation	[49]
24	Stavudine	Ethyl cellulose, di butyl phthalate	solvent evaporation	[50]

Advantages of Floating Drug Delivery System[8,9,51,52]

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery. These advantages include:

1. FDDS can remain in the stomach for several hours and therefore prolong the gastric retention time of various drugs.
2. FDDS are advantageous for drugs meant for local action in the stomach eg: Antacids.
3. FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhea to keep the drug in floating condition in stomach to get a relatively better response.
4. FDDS improves patient compliance by decreasing dosing frequency.
5. Bioavailability enhances despite first pass effect because fluctuations in plasma drug concentration are avoided; a desirable plasma drug concentration is maintained by continuous drug release.
6. Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
7. The FDDS are advantageous for drugs absorbed through the stomach eg: Ferrous salts, Antacids.
8. Improved drug absorption of drugs because of increased GRT and more time spent by the dosage form at its absorption site.
9. FDDS improves patient compliance by decreasing dosing frequency.
10. Site-specific drug delivery.

Limitations of Floating Drug Delivery Systems[5,15]

1.Drugs which are irritating the gastric mucosa are also not suitable.

2.The drug substances that are unstable in the acidic environment of the stomach are not suitable candidates to be incorporated in the systems.

3.Not suitable for drugs that have solubility or stability problem in GIT.

4.The drugs that are significantly absorbed through out gastrointestinal tract, which undergo significant first pass metabolism (e.g. Nifedipine, propranolol), are not desirable candidate.

5.The ability to float relies on the hydration state of the dosage form. Therefore, a high level of fluid in the stomach is required for drug delivery to float and work efficiently.

CHARACTERIZATION OF FLOATING MICROSPHERES

Micromeritic properties: Floating microspheres can be characterized by their micromeritic properties such as particle size, tapped density, compressibility index, true density and flow properties including angle of repose. The particle size can be determined by optical microscopy; true density can be determined by liquid displacement method; tapped density and compressibility index are calculated by measuring the change in volume using a bulk density apparatus; angle of repose can be determined by fixed funnel method. The hollow nature of microspheres can be confirmed by scanning electron microscopy.[13]

Particle Size and shape: Scanning electron microscopy (SEM) provides higher resolution in contrast to the light microscopy. The most widely used procedures to visualize microparticles are conventional light microscopy and scanning electron microscopy (SEM). Both can be used to determine the shape and outer structure of multiparticulate.

Floating behavior: The characterization of sodium alginate microspheres were performed with swelling index technique. Floating microspheres should be placed in 100 ml of the simulated gastric fluid (SGF, pH 2.0) containing 0.02% w/v Tween 20. The mixture was stirred at 100 rpm with a magnetic stirrer. After 8 hours, the layer of buoyant microspheres was pipetted and separated by filtration. Particles in the sinking particulate layer were separated by filtration. Particles of both types were dried in a desiccator until constant weight was achieved. Both the fractions of microspheres were weighed and buoyancy was determined by the weight ratio of floating particles to the sum of floating and sinking particles.

$$Buoyancy\ (\%) = \frac{Wf}{Wf + Ws} \times 100$$

where, Wf and Ws are the weights of the floating and settled microparticles, respectively.[23]

Percentage drug entrapment

Efficiency of drug entrapment for each batch was calculated in terms of percentage drug entrapment as per the following formula:

$$\%\ Drug\ entrapment = \frac{Practical\ drug\ loading}{Theoretical\ drug\ loading} \times 100$$

In-vitro drug release study: The release rate of floating microspheres is determined using United States Pharmacopoeia (USP) XXIII basket type dissolution apparatus. A weighed amount of floating microspheres equivalent to 50 mg drug is filled into a hard gelatin capsule (No. 0) and placed in the basket of dissolution rate apparatus. 500 ml of the SGF containing 0.02% w/v of Tween 20 is used as the dissolution medium. The dissolution fluid is maintained at 37 ± 1° at a rotation speed of 100 rpm. Perfect sink conditions prevailed during the drug release study. 5ml samples are withdrawn at each 30 min interval, passed through a 0.25 µm membrane filter (Millipore), and analyzed using LC/MS/MS method to determine the concentration present in the dissolution medium. The initial volume of the dissolution fluid is maintained by adding 5 ml of fresh dissolution fluid after each withdrawal.[12]

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.

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly complex and variable procedure. Prolonging gastric retention of the dosage form extends the time for drug absorption. Floating controlled drug delivery systems are employed to solve this problem. Floating microspheres have shown great potential for gastroretention and provide an efficient means of enhancing bioavailability and controlling the release of many drugs.

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