



A REVIEW ON APPROACH OF USING FLOATING MICROSPHERES IN GASTRORETENTIVE DRUG DELIVERY SYSTEMS

Miss. Shamal SatishPatil*, Prof. Rajendra K. Surawase, Miss. Vaishali Vijay Pagar, Miss. Aishwarya Gulab Bhamare, Miss. Pratibha Kadu Pagar

(Department of Pharmaceutics)

Loknete Dr. J. D. Pawar College of Pharmacy, Manur Tal – Kalwan Dist – Nashik (423501), Maharashtra, India

Abstract

Several obstacles must be overcome for oral drug delivery systems in order to sustain drug release and prolong the time the medication remains in the gastrointestinal tract until it has been completely ingested. After a certain amount of time, fully released. When the stomach is empty, a process known as gastric emptying takes place. It could be quite helpful for athletes who are experiencing gastrointestinal issues. There is a window for nutrient absorption in the upper small intestine. Drugs that are poorly soluble or unstable in intestinal fluids might benefit greatly from floating microspheres that improve drug retention and enable prolonged action in the stomach. Floating drug delivery systems (FDDS) float in the stomach for a long time because of their lower bulk density than gastric fluids. Due to the possibility that floating microspheres in the stomach may lengthen a medication's retention time, the effects of the drug may remain longer. As a result, a longer drug retention time and a slower metabolism are required to assure long-term efficacy.

FDDS dose forms are effective in situations of constipation and hyperactive bowel movement to elicit a significantly better reaction. Floating drug delivery systems (FDDSs) are helpful in these circumstances. They are anticipated to float on the stomach's contents for a considerable amount of time. Gastro retentive dosage forms are available in a variety of formats, such as tablets and capsules. Hollow microspheres are garnering a lot of interest due to their numerous potential uses in medicine delivery. Due to the drug substance being uniformly dispersed throughout the stomach juice, this prevents the drug from being released too soon. This review's objective is to examine floating microspheres approach in Gastro-retentive Drug Delivery System

Keywords

Floating drug delivery systems (FDDSs), Floating microspheres, Gastro retentive dosage forms, Gastro-retentive Drug Delivery System.

Introduction

The oral route of administration of drug is the one that is most frequently used for therapeutic pharmaceuticals due to its low cost and simple administration, which promotes high patient compliance. Oral medication delivery methods make up more than half of all drug delivery systems on the market. Important medications from a variety of pharmacological categories that have poor oral bioavailability due to insufficient absorption and/or degradation in the gastrointestinal (GI) tract are only seldom administered orally.^[1]

To sustain drugs in the stomach, floating drug delivery systems (FDDS) were developed. These devices are useful for medications that have poor intestinal fluid solubility and stability. Making the dose form less dense than the gastric juices allows it to float on them, which is the principle underpinning FDDS. FDDS are hydrodynamically controlled low-density systems that have enough buoyancy to float over the contents of the stomach and stay buoyant there without significantly slowing down the gastric emptying process. With the drug's release, the stomach's residual system is emptied.^[2]

Gastro-retentive Drug Delivery System

Scientific and certification literature has made it evident that the stomach is becoming more focused in the present. Today, research for both educational and commercial purposes lasts for a very long time. Running time of gastric occupancy may be the most practical for obtaining a long and predictable medication delivery plane in a GI system.

New and crucial treatment choices will be made available to us due to gastro-retentive dosage forms. As a result, GI technique offers the ability to control the positioning of DDS in a certain area, especially when used as an absorption window for drug demonstration. The pace of soaking the opinions has been impacted by a personal touch of DDS that is capable of greater drug absorption and increases the capacity of oral regulated gastric perception. Because the dose forms can be drawn from dry upper sections that are typically irregular and inadequate, the gastro-intestinal system in these medications cannot be maintained in an equal proportion over the length of the gastro-intestinal system.^[3]

The gastro retentive drug delivery system (GRDDS) aims to target the site-specific release of medicines in the upper gastrointestinal tract (GIT) to produce local or systemic effects by extending the length of gastrointestinal residency. Gastro retentive systems can stay in the gastrointestinal region for several hours, which improves the drug's bioavailability, lowers drug waste, and helps make poorly soluble medications more soluble in environments with higher pH levels.^[4]

Gastric retention impacting factors

Density

The dosage form's density should be lower than the stomach contents' (1.004g/ml) density.

Size

According to reports, dosage form units with a diameter of more than 7.5 mm had a higher GRT compared to those with a diameter of 9.9 mm.

Shape

In comparison to other forms, the dosage form with a tetrahedron shape and ring shape devices that have flexural moduli of 48 and 22.5 kilo pounds per square inch (KSI) are said to have greater GRT, 90 to 100% retention at 24 hours.

Unfed or Fed State

Fasting-related GI motility is characterised by bursts of vigorous motor activity or migrating myoelectric complexes (MMC), which happen around every 1.5 to 2 hours. The MMC removes undigested matter from the stomach, hence the GRT of the unit can be anticipated to be quite brief if the timing of formulation delivery and the MMC are coordinated. MMC is delayed and GRT is significantly longer in the fed condition, however. Compared to single unit dosage forms, multiple unit dosage forms have a higher margin of safety against dosage form failure, a more predictable release profile, and minimal performance impairment from unit failure. They also allow co-administration of units with different release profiles or containing incompatible substances.

Kind of food consumed

Feeding indigestible polymers of fatty acid salts can cause the stomach's motility pattern to transition to a fed state, slowing down gastric emptying and extending the time that the medicine remains in the body.

Caloric Value

With a meal that is rich in proteins and lipids, GRT can be extended by 4 to 10 hours.

Frequency of feeding Because to the low frequency of MMC, the GRT might increase by more than 400 minutes when many meals are given instead of only one.

Gender

In general, females empty their stomachs more slowly than males. Depression causes a slowdown in stomach emptying rates whereas stress speeds them up.

Age

The GRT is noticeably longer in older persons, especially those over 70.

Diseased condition of the person

Gastric retention is also influenced by biological variables, such as Crohn's disease, gastrointestinal disorders, and diabetes. concurrent medication administration Atropine, propentheline, codeine, and prokinetic drugs like metoclopramide and cisapride are examples of anticholinergics.^[5]

Table 1 - Drugs Used to Develop Gastroretentive Dose Forms^[6]

Sr. No.	Dosage form	Drug
1.	Floating microspheres	Tranilast, Terfenadine, Ibuprofen, Griseofulvin, and Aspirin.
2.	Floating granules	Indomethacin, Prednisolone, and diclofenac sodium
3.	Films	Cinnarizine.
4.	Floating capsule	Diazepam, Furosemide, Misoprostol, Chlordiazepoxide Hydrogen Chloride,

Fundamental Physiology of the Gastrointestinal Tract

The stomach is anatomically separated into three sections: the fundus, body, and antrum (pylorus). The body and fundus, which make up the proximal portion, serve as a storage area for undigested matter, whereas the antrum is the primary location for mixing motions and serves as a pump for stomach emptying by pushing activities. According to reports, fasting healthy people have an average pH of 1.1-1.5. Yet, due to the buffering ability of proteins, the pH may increase to values in the range of 3.0 to 4.0 when food enters the stomach. Nonetheless, basal gastric secretion in women is marginally lower than in males in the fasting state.

In both the fed and fasted phases, the stomach empties. Yet, the two states' motility patterns are different from one another. An interdigestive series of electrical events that cycle through the stomach and intestine every two to three hours take place during the fasting state. This is known as the migrating myoelectric cycle (MMC), which is further broken down into the following 4 phases:

- Rare contractions last for 30 to 60 minutes during Phase I (Basal Phase).
- Phase II (Preburst Phase) lasts 20 to 40 minutes and is characterised by sporadic contractions and action potentials. The intensity and frequency steadily rise as the phase goes on.
- The duration of Phase III (Burst Phase) is 10 to 20 minutes. It contains brief, recurring contractions that are strong and frequent. This wave is responsible for sweeping all undigested matter from the stomach into the small intestine. Another name for it is the housekeeping wave.
 - Phase IV, which takes place between phases III and I of two successive cycles, lasts 0 to 5 minutes.^[7]

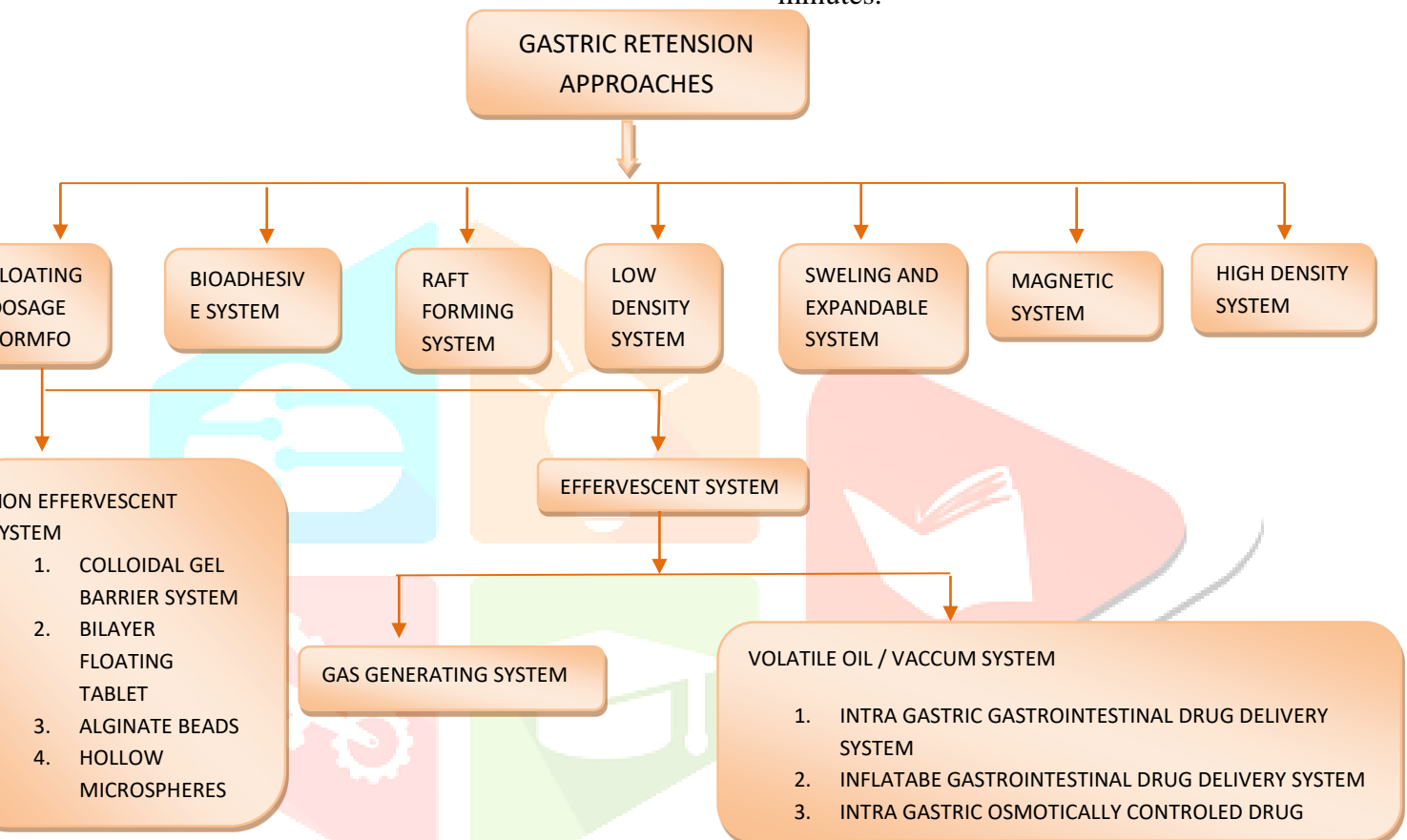


Figure 1: Several methods of gastric retention^[8]

FLOATING DRUG DELIVERY SYSTEM

As a hydrodynamically controlled system, floating medication delivery systems are also known. Due to its low density, the medication has a high degree of buoyancy and can float in the stomach's gastric fluid without slowing down the stomach's rate of emptying. It floats over the contents of the stomach as the medicine is released gradually at the proper rate, extending the duration that the food remains in the stomach and minimising changes in the drug's concentration in the blood. These kinds of medications often have few unwanted side effects and good bioavailability with long-lasting effects.

Incomplete drug release from the drug delivery system might result in reduced effectiveness of supplied dose due to the average gastric emptying period in humans, which is typically 2-3 hours through the major absorption zone (stomach and upper part of intestine). The treatment of gastrointestinal illnesses benefits

from lower dosage and fewer adverse effects. suitable dosage forms for medications whose absorption occurs largely in the stomach.^[1]

FLOATING DRUGS DELIVERY SYSTEM FRAMEWORK

There have been several attempts to prolong the retention duration by keeping the dosage form in the stomach. These attempts include the introduction of floating dosage forms, including those that produce gas, swell or expand, are mucoadhesive, high-density, or have changed shapes, as well as devices that delay stomach emptying and drugs that delay gastric emptying when taken together. The floating dose formulations have been the most widely employed of these. Floating drug delivery systems (FDDS) float in the stomach without slowing down the gastric emptying rate since their bulk density is lower than that of gastric fluids. The medication leaves the body at the desired pace but slowly. The stomach's residual system is emptied following medication release. As a result, the GRT is raised and the oscillations in plasma drug concentration are better managed. In order to avoid the negative effects of unforeseen intragastric buoyancy capability fluctuations, this equipment aids in improving FDDS with regard to stability and endurance of floating forces produced.

RISK FACTORS OF FLOATING DRUGS DELIVERY SYSTEMS

- To float and function effectively, drug delivery needs a lot of fluid in the stomach.
- Drugs with stability and solubility issues in the gastrointestinal tract are not good choices for these kinds of systems.
- It is also not advisable to take medications that irritate the stomach mucosa.
- Drug compounds that are unstable in the stomach's acidic environment are not good candidates to be added to the systems.^[9]

Types of microspheres

Magnetic microspheres

The novel drug delivery system (magnetic Ferro) uses magnetic microspheres, which are molecules above molecules and small enough to rotate within capillaries without causing occlusive blockage (4 m), as holders for the drugs as they are taken up by the microvessels and expelled. magnetic field of 0.5-0.8 Tesla applied to nearby tissues

Bioadhesive microspheres

Certain forms of microspheres, known as bioadhesive microspheres, have lengthy lodging times in the application place, cause close contact with the site of absorption, and result in improved therapeutic activity.

Floating microspheres

Low intensity systems called intestinal floating tiny spheres can float through stomach contents and stay in the stomach for a long period without slowing down gastric emptying. The medication is gradually delivered at the necessary frequency.

Microspheres with radioactivity

Distribute a height ray dosage to the desired areas without harming the tissues in the natural surroundings. Into the arteries leading to the tumours are injected. Radiation-emitting microspheres come in three different types: $[\gamma]$ emitters, $[\alpha]$ emitters, and $[\beta]$ emitters.

Microspheres made of polymers

Due to their increase characteristic grade of swelling with a watery middle, a result of gel formation, biodegradable polymeric microspheres are those that contain biodegradable polymers that prolong a lodging duration during contact with snotty membrane. The continual focus of the polymer and the release pattern regulate the average and range of drug reals. Artificial polymeric microspheres, which are composed of synthetic polymers, are utilised as fillers, bulking agents, embolic particles, drug delivery composites, and other things.

Technique of preparation for microspheres.

1. Single-emulsion technique
2. Double-emulsion method
3. Quassi emulsion solvent diffusion
4. Extraction of solvents
5. Technique for polymerization
6. Spray congealing and drying
7. Phase separation coacervation technique

1. Single-emulsion technique

By using a single emulsion process, natural polymers including proteins and carbohydrates are transformed into microspheres. In this process, the polymers are first dissolved in an aqueous medium before moving on to an oily one. This will cause the aq. polymer solution to form little globules. The second phase involves cross-linking using a chemical agent, such as glutaryldehyde, formaldehyde, or di acid chloride, or by adjusting the temperature.

2. Double emulsion method

This technique is appropriate for water-soluble medications, proteins, vaccines, and peptides made of natural or artificial polymers. The creation of several emulsions, including W/O/W, was a part of the microspheres formulation. The primary emulsion is created when the water-soluble medicines are first dissolved in the water phase, followed by polar organic solvent with constant stirring. Before adding this primary emulsion to the PVA aqueous solution, it is homogenised. This results in the creation of a double emulsion. Afterwards, either solvent evaporation or solvent extraction was used to remove the solvent from this emulsion

3. Quassi emulsion solvent diffusion

In this procedure, the drug and polymer are dissolved in an organic solvent, and the resultant combination is then added to an aqueous solution of PVP (0.2%) while being vigorously stirred (500-800). The drug-polymer solution was transformed into droplets, then the solvent was evaporated to solidify the resulting microspheres.

4. Extraction of solvents

This procedure required dispersing a polymer solution in an aqueous phase and evaporating an organic volatile solvent from it. The rate of solvent evaporation depends on the temperature of the water, the volume of the emulsion, and the solubility profile of the polymers.

5. Technique for polymerization

Originally, this method has been employed to create microspheres. Broadly categorised as:

- ❖ Interfacial polymerization
- ❖ Normal polymerization

Interfacial polymerization

Interfacial polymerization is the process by which different monomers react at the boundary between two immiscible liquid phases to create a polymer film that basically encases the dispersed phase.

Normal polymerization

In this process, the catalyst or initiator is dissolved in bulk with the monomer or mixture of monomers, and polymerization is often started by heating. Microspheres of polymer were obtained. During the polymerization process, drugs are loaded. Several methods, including as bulk, suspension, precipitation, emulsion, and micelle polymerization processes, are used in normal polymerization. Pearl polymerization, which involves heating the monomers as droplets in continuous phase, is another name for suspension polymerization. Bulk manufacturing produces pure polymers.

6. Spray congealing and drying

These are the commercial processes for creating microspheres. This approach involves dissolving polymers in an organic volatile solvent like chloroform, acetone, or dichloromethane before adding the medication to the polymer solution. The atomization of this dispersion in the heated air stream results in the creation of tiny droplets or fine mist. Microspheres with a size range of 1 to 100 m are created as a result of the instantaneous solvent evaporation from these droplets; solvent residue is removed by vacuum drying, and particles are sorted using a cyclone separator. Spray drying and spray congealing are the terms used to describe the processes, depending on whether the solvent is removed or the solution is cooled.^[10]

7. Phase separation coacervation technique

The major phases in this technique are as follows

Step 1: A coating polymer solution is used to spread the core material.

Step 2: In the liquid production vehicle phase, the coating is applied by carefully controlling the physical mixing of the coating solution and the core material.

Step 3: Rigidize the coated polymer using the techniques below.

✓ Thermal Change

Drug is added to the aforementioned solution while agitating vigorously to dissolve the polymer in cyclohexane at 80°C. By maintaining the microsphere in an ice bath, the temperature may be reduced. Cyclohexane is used twice to wash and dry the product.

✓ Non-Solvent Addition

The medication is first dissolved in toluene that contains propyl isobutylene in a closed beaker while being stirred for six hours at 500 rpm. The resulting solution is continuously stirred into benzene. The microcapsules are cleaned with n-hexane and allowed to air dry for two hours.

✓ Addition of Polymers

By dissolving the polymer (ethyl cellulose) in toluene and adding methylene blue as the core ingredient, microspheres are created. The addition of liquid polybutadiene produces coacervation. By including a nonsolvent, polymer coating is made solid (hexane). The finished item is cleaned and let to air dry.

✓ Addition of Salt

Corn oil is used to dissolve the oil-soluble vitamin before adding it to the gelatin solution at 50°C. The addition of sodium sulphate causes coacervation, which results in a homogeneous coating of gelatin. The microspheres are collected, cleaned, refrigerated, and dried.

✓ Interaction of Polymers

In this method, equal volumes of an isoelectric point 8.9 aqueous solution of gelatin and gum Arabica are combined to create a homogenous polymer solution. The aforementioned solution is warmed to 40–45°C, adjusted to a pH of 4.5, and diluted with water two times their volume. Under these circumstances, the oppositely charged macromolecules interact and experience coacervation. The polymer solution is added, and the liquid core material is thoroughly mixed, all while maintaining the warm temperature.

After that, the mixture is cooled to 25 °C and chilled to 10 °C to rigidify the coating.^[11]

Applications of floating microspheres

1. For drugs with so-called "absorption windows," such as antiviral, antifungal, and antibiotic agents (sulphonamides, quinolones, penicillins, cephalosporins, aminoglycosides, and tetracyclines), floating microspheres can be used as carriers. These drugs are only absorbed from very specific sites of the GI mucosa.
2. Non-steroidal anti-inflammatory medication hollow microspheres are excellent for regulated release and lessen the main side effect of stomach irritability. For rheumatoid arthritis patients, floating microspheres of indomethacin is particularly helpful.
3. Floating microspheres are particularly good at delivering insoluble and sparingly soluble medicines. It is well recognised that as a medication's solubility declines, the amount of time available for drug dissolution reduces, and as a result, transit time becomes an important factor influencing drug absorption. Hollow microspheres may help weakly basic medications that are poorly soluble at an alkaline pH avoid the possibility that solubility will become the rate-limiting stage in release by limiting such pharmaceuticals to the stomach. Drugs that are effectively absorbed through the stomach, like verapamil hydrochloride, benefit from positioned gastric release.
4. Hollow microspheres can significantly enhance stomach pharmacotherapy through local drug release, resulting in high drug concentrations at the gastric mucosa, which eliminates *Helicobacter pylori* from the submucosal tissue of the stomach and makes it possible to treat stomach and duodenal ulcers, gastritis, and oesophagitis.

Merits of floating microspheres:

1. Despite the first pass effect, bioavailability is increased because continuous drug release helps to maintain a desired plasma drug concentration and prevents variations in drug concentration.
2. These microspheres are superior to single-unit floating dosage forms because they distribute medications consistently and there is no chance of dose dumping.
3. Improved absorption of medications that just dissolve in the stomach.
4. It is possible to administer drugs to the stomach in a site-specific manner.
5. Gastric irritation can be avoided because of the sustained release effect.
6. The therapeutic effects of medicines with short half-lives can be improved. The basic issue with floating micro spheres is the reproducibility of the formulation's particle size. ^[12]

The drawbacks of microspheres

1. The pace of controlled release of microspheres may vary depending on internal or external circumstances, such as diet, the speed at which it travels through the stomach, the rate at which mucin changes, etc.
2. There are variations in release from one dose form to another.
3. In the case of parenteral microspheres, little medication loading is performed.
4. When microspheres are administered parenterally, it might be challenging to entirely eliminate the carrier from the body.
5. Microspheres delivered by the parent may interact or combine with blood components.
6. It is possible to alter the formulation's release.
7. Any degradation of the release pattern might potentially be harmful. ^[13]

TABLE 2 :Polymers used in microspheres^[14]

POLYMER	ACTION
Modified starch, HPMC, Carbopol 974P	Slower release of drug
Ethyl Cellulose	Controlled release for longer period of time.
PLGA, Chitosan	Vaccine delivery.
PLA, PLGA, Starchcyanoacrylateetc(PEG-) liposomes	Drug delivery without toxic side effects
Magnetic polystyrene microspheres	Specific cell labelling
Polymer resins such as Agarosepolyacrolone, sephadex	Affinity chromatography
Chitosan coated PIGA microspheres	Targeted drug delivery
Polyvinyl alcohol, polyacrylamide	Adsorption of harmful substances in blood

ASSESSMENT OF FLOATING MICROSPHERES

Surface morphology and shape,Percentage of yield ,Bulk density,Tapped density, Carr's (compressibility) index ,The Hausner 's ratio ,Angle of contact,Swelling studies , Drug entrapment efficiency (DEE), Studies on stability , In vitro drug release study , Evaluation of in-vitro buoyancy , In-vivo identification were all carried out as basic and derived micrometric properties.

Surface morphology and shape

Microspheres scattered on one side of an adhesive stub to provide samples for scanning electron microscopy (SEM) investigation. The microspheres then gold-coated in preparation for microscopy. The size and shape of the microspheres next examined using a scanning electron microscope.^[15]

Percentage of yield

Continuous stirring was used to determine the floating microspheres' % yield for the medication. The removal of the solvent causes polymer to precipitate at the oil/water interface of the droplets, creating a hole and giving them a hollow interior that gives them their floating capabilities. For the creation of such systems, cellulose acetate, chitosan, polyacrylates, polyvinyl acetate, carbopol, agar, polyethylene oxide, and polycarbonate have all been explored.^[16]

Bulk density

The proportion of the powder's total mass to its bulk volume is known as the bulk density. One gramme of weighted microspheres are poured into a measuring cylinder to determine the bulk volume.

$$\text{Bulk density} = \frac{\text{Powder weight}}{\text{BulkVolume}}$$

Tapped density

The tapped density is determined by dividing the powder's total mass by its tappedvolume.^[17]

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume}}$$

Carr's (compressibility) index

The following equation was used to determine the microparticles' compressibility index (C.I.) or Carr's index value.^[18]

$$\% \text{ compressibility} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

The Hausner's ratio

The Hausner's ratio of microspheres was calculated by comparing the tap density to the bulk density using the formula:^[19]

$$\text{Hausner's Ratio} = \frac{\rho_t}{\rho_b}$$

Angle of contact

The angle of contact is measured in order to ascertain a microparticulate carrier's wetting capacity. It influences whether microspheres are hydrophilic or hydrophobic in nature. At the interface of the solid, air, and water, the angle of contact is measured. A droplet is placed in a circular cell that is put above the objective of an inverted microscope to determine the angle of contact. Within a minute of the microspheres being deposited, the contact angle is measured at 200C.^[20]

Swelling studies

The analysis was carried out by soaking the known weight of microspheres in 0.1 N HCl for the required duration at 37.5 °C. At various time periods, the microspheres are removed after being given opportunity to swell.^[21]

$$\text{Swelling Ratio} = \frac{\text{Weight of Wet Formulation}}{\text{Weight of Formulation}}$$

Drug entrapment efficiency (DEE)

By shattering the microballoons and extracting with aliquots of the right solvent repeatedly collected, the amount of drug entrapped is calculated. The extract is then transferred to a 100 ml volumetric flask, and the required solvent is used to create the final volume. The solution is filtered, and a spectrophotometer is used to measure the absorbance in comparison to the proper blank.^[22]

$$\text{DEE} = \frac{\text{Amount drug present}}{\text{Amount of drug taken}} \times 100$$

Studies on stability

By putting the microspheres in a glass container with a screw-on lid and keeping them in the following conditions:

- A humid environment
- The ambient temperature is 27±2 °C.
- Oven temperature (40±2 °C)
- Refrigerator (5 °C -80C) (5 °C -80C).

Analyses of the microsphere's drug content were conducted throughout a 60-day period.^[23]

In vitro drug release study:

USP XXII paddle type dissolution apparatuses can be used for in vitro dissolution research.

The medication dose-equivalent microspheres are added to 900 ml of the dissolving media, which is stirring at 100 rpm at 37.0°C. To keep the sink condition, 0.1 N HCl (pH 1.2) with 0.2% Tween 20 was used as the dissolving media. At intervals of 1, 2, 4, 6 and 8 hours, aliquots of 10 ml were taken out. To keep the sink state, an equivalent volume of dissolving media was substituted. Using a 0.45 µm syringe filter, the withdrawn materials were filtered. To measure the drug concentration, spectrophotometric analysis was performed on the samples at 239 nm.^[24]

Evaluation of in-vitro buoyancy

900 cc of 0.1 N hydrochloric acid containing 0.02% tween 80 was placed in a USP XXIV dissolving equipment type II (Electro Laboratories, Bombay) and covered with 300 mg of microspheres. A paddle that rotated at 100 rpm was used to stir the medium. Microspheres' settling and floating parts were retrieved separately. After drying, the microspheres were weighed. The ratio of the mass of the microspheres that stayed floating to the overall mass of the microspheres, represented as a percentage, was used to compute buoyancy percentage.^[25]

In-vivo identification

According to the results of the in vitro release research, the best microsphere formulation for the in vivo experiments was chosen. After being purchased, albino rats underwent a 10-day acclimatisation period before the experiment will be carried out.^[26]

Klausner et al. used unfolding polymeric membranes with expanded dimensions and high stiffness to construct a new controlled release GRDDS of levodopa. The beagle dogs were given a carbidopapretreatment for the in vivo research. The formulated formulation was given, and an X-ray was used to pinpoint where in the gastrointestinal tract the dosage form was located. Also, serial blood samples were taken and tested for the drug's active ingredient. The therapeutic concentrations of levodopa (>500 ng/ml) were reported to be maintained over a 9-hour period by the optimised controlled release GRDDS of levodopa. In comparison to oral solution and non-GR controlled release particles, the mean absorption period was significantly extended.^[27]

Jain et al. developed the hypoglycemic drug repaglinide as a floating microsphere. Male albino rabbits weighing 2.2 to 2.5 kg were used for the in vivo tests. In order to acclimatise the rabbits, they were housed in the animal home for a week and fed a set standard diet. Six rabbits each from two groups of twelve were fasted for 24 hours. Animals in one group were given a Rapilin pill (a commercial medication) containing 1 mg of RG, whereas another set of animals received RgFMCS4 with the same amount of RG. Throughout the trial and while the subjects were fasting, unlimited water was provided. The therapy was supplied to the rabbits using an oral cannula without the need for anaesthesia either during or before the procedure. They easily absorbed the formulation after swallowing it. Over the course of the trial, blood samples (2 ml) were taken from the marginal ear vein into heparinized centrifuge tubes shortly before to dosing as well as at 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 10, and 24 h. The blood samples were taken as described above, and then put into a series of graded centrifuge tubes with 0.4 ml of a 2.5% w/v sodium citrate solution. The samples were centrifuged for 5 minutes at 2500 rpm. A different set of sample tubes were used to transfer the plasma, and it was then refrigerated until analysis. Plasma from one undosing was maintained as a blank sample. 0.25 µm membrane filter was used to filter the sample (Millipore). The HPLC technique previously described was used to determine the Rg levels in blood samples.^[28]

Conclusion

Drug absorption through the gastrointestinal tract is a highly unpredictable process. A possible treatment for stomach retention that might result in a site-specific, regulated medication release and have a significant effect on health care is the floating microsphere. The design of innovative oral formulations is made possible by these technologies, further expanding the limits of pharmaceutical research and development. Also, the most recent advancements in pharmaceutical research will undoubtedly offer viable opportunities for the formation of unique and efficient methods in the development of these potential drug delivery systems.

Although there are several issues that must be resolved in order to achieve extended gastric retention, several businesses are concentrating on commercialising this method. The control in this situation. The next ten years may be devoted to GIT transit time, with new technologies perhaps emerging as a consequence. Many therapy options are available for patients, who can profit from them. This article will help by giving a quick summary of the floating microsphere preparation and assessment parameters. The study of floating microspheres will be continued by research scholars .

Reference

- 1.Kumar P, Khairya D, Teotia D, Rajpoot V. Floating drug delivery system: an updated review. International Journal of Current Innovations in Advanced Research.2022 Nov 5:8-16.
- 2.Niharika MG, Krishnamoorthy K, Akkala M. Overview on floating drug delivery system. Int J Appl Pharm. 2018;10(6):65-71.
- 3.Rani R, Kumar M, Yadav N, Bhatt S, Malik A, Kumari B, Sangeeta D, Kumar A, Meerpur R. Recent Advances in the Development of Floating Microspheres for the Treatment of Gastric Ulcers.Recent Advances in the Development of Floating Microspheres for. 2020;29(5):3613-27.
- 4.Rashmitha V, Pavani S, Rajani T. An Update on Floating Drug Delivery System: A Review.
5. Mali AD, Bathe RS, Patil MK. Floating microspheres: a novel approach in drug delivery system. Science and Technology. 2015;1(5):134-53.
- 6.Patil C, Baklilwal S, Rane B, Gujrathi N, Pawar S. Floating microspheres: A promising approach for gastric retention. International journal of pharma research and developments. 2011;2:12.
- 7.Shah K, Sharma PK, Bhandari A, Garud A, Garud N. FLOATING MICROSPHERES AS GASTRORETENTIVE DRUG DELIVERY SYSTEMS: A REVIEW.
- 8.SAINI S, ASIJA R, GOYAL A. Floating Microsphere as Gastro Retentive Drug Delivery System: An Updated Review. Tropical Journal of Pharmaceutical and Life Sciences. 2022 Apr 27;9(2):21-9.
- 9.Lodhi DS, Verma M, Golani P. FLOATING MICROSPHERES A NOVEL APPROACH IN FLOATING DRUG DELIVERY SYSTEM A REVIEW.
- 10.Tiwari R. MICROSPHERES: A UNIQUE DRUG DELIVERY SYSTEM WITH IMMENSE BIOPHARMACEUTICAL SOLICITATIONS.
- 11.Sudheer P, Kumar H, Thomas L, Nethravathi DR. Floating microspheres-an excellent approach for gastric retention. Journal of Pharmaceutical Research. 2015 Dec 1;14(4):71-80.
- 12.Mukund JY, Kantilal BR, Sudhakar RN. Floating microspheres: a review. Brazilian Journal of Pharmaceutical Sciences. 2012;48:17-30.

- 13.Srivastav S, Kumar K, Joshi A, Teotia D, Ikram I. An updated review on microspheres: a suitable drug carrier in sustained release drug delivery. *International Journal of Indigenous Herbs and Drugs*. 2022 Apr 18:40-8.
- 14.Abass KH, Kadim AM, Mohammed SK, Agam MA. Drug Delivery Systems Based on Polymeric Blend: A Review. *Nano Biomed. Eng.* 2021 Oct 1;13(4):p414-424.
- 15.FC M, Kamath KK, Shabaraya AR. Development of Gastro Retentive Floating Microspheres of Roxatidine Acetate HCl By Emulsion Solvent Diffusion Technique. *Technology*. 2019;9(4):530-7.
- 16.Kumar JV, Manish J. Microballoons for drug delivery: a review. *Asian Journal of Pharmaceutical Research and Development*. 2013 Jan 1:7-17.
- 17.Arumugam KA, Borawake PD, Shinde JV. Formulation and evaluation of floating microspheres of ciprofloxacin by solvent evaporation method using different polymers. *International journal of pharmacy and pharmaceutical sciences*. 2021;13(7):101-8.
- 18.Pujara ND, Patel NV, Thacker AP, Raval BK, Doshi SM, Parmar RB. Floating microspheres: A novel approach for gastro retention. *World journal of pharmacy and pharmaceutical sciences*. 2012 Aug 1;1(3):872-95.
- 19.Chainesh S, Chitan A, Vinod R. An Overview on Gastroretentive Floating microspheres. *International Journal*. 2012;2(2):01-8.
- 20.Singh C, Purohit S, Singh M, Pandey BL. Design and evaluation of microspheres: A Review. *Journal of drug delivery research*. 2013;2(2):18-27.
- 21.Birajdar AA, Deshmukh MT, Shete RV. A Review on Gastro-Retentive Floating Microspheres. *Journal of Drug Delivery and Therapeutics*. 2021 Feb 15;11(1-s):131-8.
- 22.Gurung BD, Kakar S. An overview on microspheres. *Int J Health Clin Res*. 2020;3(1):11-24.
- 23.Srikar G. Floating microspheres: A prevailing trend in the development of gastroretentive drug delivery system. *Asian Journal of Pharmaceutics (AJP)*. 2018 Nov 11;12(04).
- 24.Jagtap YM, Bhujbal RK, Ranade AN, Ranpise NS. Effect of various polymers concentrations on physicochemical properties of floating microspheres. *Indian journal of pharmaceutical sciences*. 2012 Nov;74(6):512.
- 25.Kumar K, Pant NC, Ahmad S, Fateh MV, Rai AK, Verma B, Chaurasia H. Development and evaluation of floating microspheres of curcumin in alloxan-induced diabetic rats. *Tropical Journal of Pharmaceutical Research*. 2016 Oct 5;15(9):1819-25.
26. Madhavi M, Madhavi K, Jithan AV. Preparation and in vitro/in vivo characterization of curcumin microspheres intended to treat colon cancer. *Journal of pharmacy & bioallied sciences*. 2012 Apr;4(2):164.
27. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and their in vivo success: A recent update. *asian journal of pharmaceutical sciences*. 2016 Oct 1;11(5):575-84.
- 28.Jain SK, Agrawal GP, Jain NK. A novel calcium silicate based microspheres of repaglinide: in vivo investigations. *Journal of controlled release*. 2006 Jun 28;113(2):111-6.