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Floating Microballoons: A Consistent Development in Gastro-Retentive Drug Delivery Systems

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ABSTRACT
For the majority of patients, oral administration is the gold standard. The microballoon is a novel pharmaceutical device that floats medication to the stomach for retention. Their gastric retention drug delivery system (GRDDS) enhances the absorption of medications and lessens stomach discomfort. Because floating microspheres have the potential to transport medications to the stomach, they are widely used. One type of non-effervescent medication delivery method that can remain in the GI tract is a floating or hollow microsphere. Hollow microspheres are spherical, coreless particles with an ideal size range of 1,000 micrometres that are made from powdered free-flowing proteins or synthetic polymers. Because microballoons float and are evenly spaced throughout the stomach, they prolong the release of medications and prevent fluctuations in gastric emptying. Its floating synthetic polymers function in capsules, tablets, and powders. The hollow interiors of the microballoons improve mucosal concentration and gastric pharmaceutical therapy while shortening the period that medications remain in the stomach. Gastro-retentive systems are low-density floating microspheres that have a lengthy half-life in the stomach. The greater the pH, the less soluble it becomes. A multiple unit system regulates these microballoons, taking preparation, temperature, and surface smoothness into account to optimum buoyancy. It relieves rheumatoid arthritis, stomach ulcers, and inflammatory bowel diseases.
Keywords: Floating Microballoons, Gastro Retention, Short half-life, Buoyant agent, Floatability.

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INTRODUCTION

Microballoons, which are drug delivery devices, have demonstrated promise as a specific therapy approach for stomach retention. A non-effervescent system composed of spherically shaped, hollow particles without a core-ideally 200 microns in size-forms the basis of microballoons. These microballoons are free-flowing powders composed of proteins and synthetic polymers. Because of their low density, microballoons can float on stomach fluid for long periods of time without irritating the gastrointestinal tract [1,2]. These easier-to-administer dosage forms made possible by cutting-edge drug delivery systems have greatly increased the safety and effectiveness of medicinal compounds. A high level of patient compliance has been noted due to the ease of handling and administering oral dosage forms. Enhancing drug absorption and release from the body in a simple, patient-compliant way that is simple to administer, predictable, repeatable, and therapeutically efficacious is the aim of oral controlled drug administration. Another option is to raise the drug's bioavailability to boost its therapeutic efficacy. Longer dosage intervals and better patient compliance are two other benefits of gastro-retentive dose forms, which greatly increase the potential release duration of the drug. Floating ion exchange resins, raft-forming systems, expansion systems, high density systems, magnetic systems, mucoadhesive or bio-adhesion systems, low density systems, and super porous hydrogels are some of the methods that can be used to develop gastric retention devices that transport medications on water [3-5].

Floating microspheres are actually spherical, centerless particles. The diameters of these free-moving particles range from 1 to 1000 µl [6]. Other names for floating microspheres are hollow microspheres,

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floating microparticles, and micro balloons. Non-effervescent hollow polycarbonate microspheres were produced by evaporating an emulsion solvent. The idea behind this GI transit product is to let it float on the stomach [7].

Floating Drug Delivery System

System types that have a low density and sufficient buoyancy to float above the stomach contents for a long period are called floating systems. By keeping the device hovering over the stomach contents, the medication is given slowly and accurately, extending the gastro retention period and reducing changes in plasma drug concentration [8].

Types of Floating Drug DeliverySystem: This system can be divided into twotypes:

a) Effervescent systems
b) Non-effervescent systems

Effervescent Systems

Volatile liquid containing systems

An inflatable chamber that is filled with an ether or cyclopentane-like gasifying liquid can be used to keep a medicine delivery system's gastric reflux temperature (GRT) constant. As a result, the stomach chamber can enlarge to its natural temperature. An alternative to the device might be a biodegradable plug made of polyethylene, polyvinyl alcohol (PVA), or any other biodeslgradable material. When the inflatable devices deteriorate, the chamber would release gas and collapse, allowing the stomach to naturally evacuate them [9].

Gas-generating Systems

Through the effervescent interactions of citric/tartaric acid and carbonate/bicarbonate salts, buoyant distribution systems release carbon dioxide, lowering the specific gravity of the system and causing it to float over water. Numerous systems repeat this procedure [10]. These buoyant systems may contain sodium bicarbonate, citric acid, swellable polymers, and polysaccharides (like chitosan).

By reacting with the acidic environment in this system, the medium helps the bicarbonate material create carbon dioxide, which reduces their bulk thickness and facilitates their ability to pass through the Gastrointestinal fluid.

Non-Effervescent Systems

In this approach, the medicament swells and reacts with the stomach fluids as it is taken, decreasing its bulk thickness before swimming across them [11].

i. System of Micro Porous Compartment
ii. Barrier colloidal gel device
iii. Beads Alginate
iv. Floating Microballoon /Hollow microsphere

Micro Porous Compartment System

This involves the placement of the drug along the pores on the top and bottom walls of the porous micro compartment. The stomach fluids begin to float after the flotation chamber traps the air.

The barrier colloidal gel apparatus (Colloidal gel barrier systems)

Because the expanded polymer traps air with a density less than one, these dosage forms float. Sheth and Tossounian first introduced the hydrodynamically balanced system (HBS) in 1975. These methods work by encasing the drugs in hydrocolloids, which allow them to float above the stomach's contents. The majority of the system is composed of matrix-forming polymers, polysaccharides (in tablet or capsule form), and hydrocolloids (a gel-forming, highly swellable sort of cellulose) (polyacrylates, polystyrene, HEC, HPMC, Nam). When the system's hydrocolloid comes into touch with gastric fluid, it hydrates and forms a colloidal gel barrier around its surface. This device features a hydro-colloidal gel form that keeps the drug floating on the stomach material [12].

Alginate beads

Sodium alginate is lowered into an aqueous solution of calcium chloride to create this calcium alginate precipitate. t aids in the formation of the permeability system, which enables it to float above the contents of the stomach for around twelve hours [13].

Floating Micro-Balloon/ Hollow Microspheres/Micro balloons

Micro-balloons seem to be non-effervescent gastro-retentive drug-delivery structures. 'Microballoons (Hollow microspheres)' are, strictly speaking, blank spherical particles without any core. These microspheres were indeed typically free flowing powders composed of proteins or synthetic materials, with a size of less than 200 micrometers. They are hollow glass in nature and are constructed of lightweight concrete or synthetic form. Using straight forward solvent evaporation or solvent diffusion / evaporation techniques, micro balloons / hollow microspheres containing medications in their other

polymer shelves were created in order to extend the dosage form's gastrointestinal retention time (GRT) [14].
Agar, low-methoxylated pectin, cellulose acetate, polycarbonate, Eudragit S, Eudragit L and calcium alginate are the polymers that are utilized. Polymer quantity, plasticizer polymer ratio, and solvent type all affect buoyancy and drug release [15].
The microsphere is a very practical buoyant system. Its hollow core is what gives microballoons their distinctive multi-input architecture and enhanced floating properties. Several novel methods were employed in their preparation, such as hot melt encapsulation, simple solvent evaporation, spray drying, spray congealing, polymerisation, and single and double diffusion emulsification. Coacervation of phases and simple emulsification diffusion were two more methods. Floatability and drug release rate are influenced by the polymer, plasticiser, and solvent types used in their manufacture. Polylactic acid, hydroxypropyl methyl cellulose, cellulose acetate, and the polymers Eudragit®S and Eudragit®L are among the many polymers used to create hollow microspheres. Two methods for controlling drug release are increasing the encapsulation efficiency and optimising the polymer to plasticiser ratio [16].
To produce a hollow internal structure in 'hollow microspheres or microballoons' filled with medication in their outer polymeric matrix, novel techniques including solvent evaporation or solvent diffusion/evaporation are used (Figure 1). The drug and an enteric acrylic polymer mixture that has been dispersed in an ethanol/dichloromethane solution are placed in an agitated Poly Vinyl Alcohol (PVA) solution that is thermally controlled at 40ºC. The organic solvent is eliminated by vigorous whirling or by raising the temperature under stress once the emulsion has stabilized. In the hollow interior chamber of a polymer microsphere holding a medication, dichloromethane and a droplet of dispersed polymer both vaporize to create the vapors phase. For more than 12 hours, the Micro-balloon floats steadily on the outside of only an acidic dissolving media that contains surfactant [17].

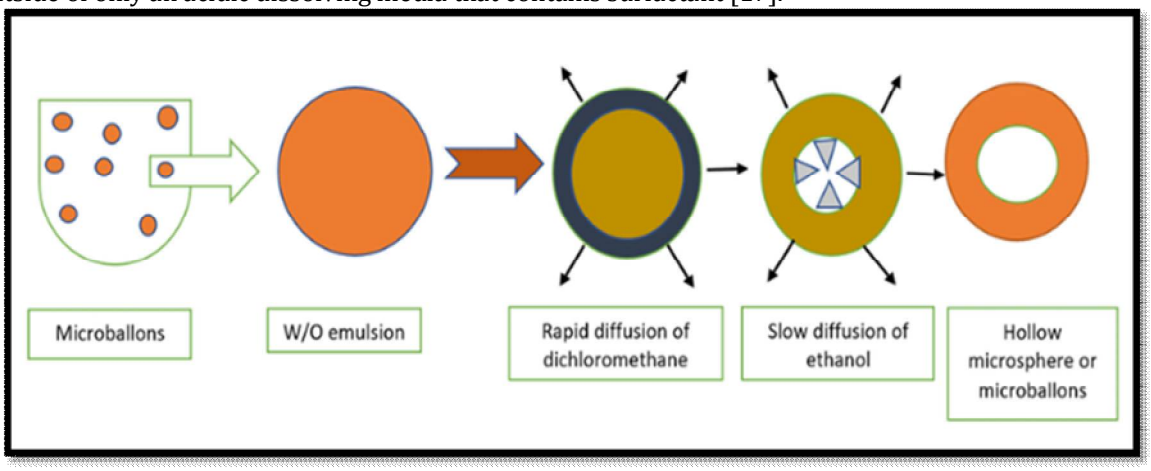

Figure 1: Formulation of floating microspheres or microballoons

Flotation Mechanisms of Microballoons (Hollow Microspheres)
To float above gastric fluid and stay in the stomach for lengthy periods of time, microballoons are low-density systems that are buoyant enough. Improving stomach retention and decreasing fluctuations in plasma drug concentration, the gadget floats above the gastric fluid and administers the medication gradually at the desired tempo. The produced microballoons showed buoyancy for more than ten hours and prolonged medication release for eight hours. A colloidal gel barrier is created when microballoons and gastric fluid come into contact. This barrier controls the flow of fluid into the device, which in turn controls the release of medications. As the outer surface of the dosage form dissolves, the gel layer is maintained by hydrating the next hydrocolloid layer. Because the expanded polymer retains air, the microspheres have buoyancy and a lower density than stomach liquid. However, only a small amount of stomach content is needed to achieve buoyancy. 'Polyethylene oxide, cellulose acetate, eudragit, hypromellose, polystyrene floatable shells, polycarbonate floating balloons, gelucire floating granules, and hollow microspheres (Microballoons) of acrylic resins' are examples of recent innovations [18]. Floating Behavior of drug in stomach is shown in Figure 2.
In order to establish a colloidal gel barrier that regulates the rate of fluid penetration into the device and, in turn, the release of the medicine, stomach acid and floating microcapsules or microballoons must come into contact. This results in a gel. The wetness of the nearby hydrocolloid layer keeps the gel layer intact as the dosage form's outer surface dissolves. The trapped air in the expanded polymer gives the

microspheres buoyancy and reduces their density. However, in order to achieve proper buoyancy, a very small amount of stomach content is required.

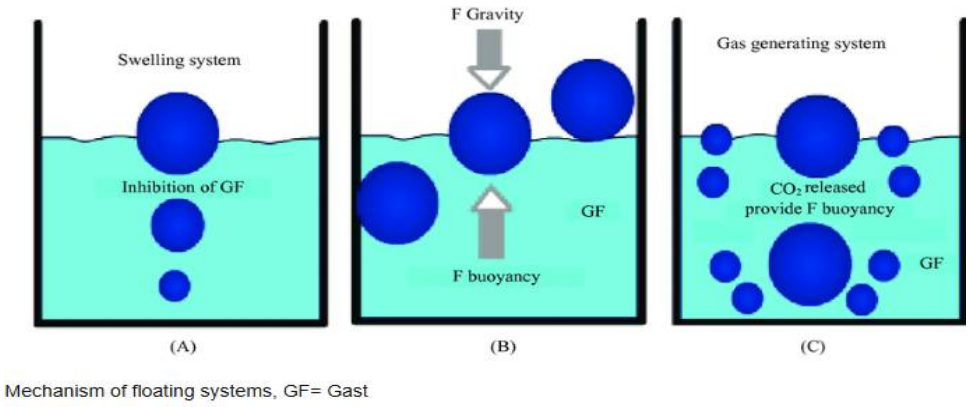

Figure 2: Floating Behavior of drug in stomach

Applications of GRDDS

Due to the upper esophageal region's limited window of absorption, gastro-retentive drug administration presents a number of potential solutions for medications with low bioavailability.

Transportation of Substances to Specific Sites

These systems work especially well for medications like furosemide, which are mostly absorbed in the stomach or the first section of the small intestine. A monolithic floating dosage form with enhanced bioavailability and a longer stomach residence duration has allegedly been created. Compared to traditional Furosemide tablets, the floating tablets produced an AUC that was more than 1.8 times higher.

Enhancing Admission

Drugs that are insoluble or only moderately soluble can be effectively delivered using floating microspheres. It is well established that transit time significantly affects pharmaceutical absorption when drug solubility decreases and drug breakdown time is limited. Weak base pharmaceutical containers may be more likely to empty at pH values higher than acidic due to their slow breakdown.

Acting as intermediaries

It is possible to effectively administer antibiotics, cephalosporins, aminoglycosides, tetracyclines, penicillin, antiviral medications, and other medications with "absorption windows" using floating multiparticles. Medication is absorbed in specific places on the gut lining. Pharmacokinetics' possible benefits The various possible advantages of floating dosage forms, which are sustained release methods, have been highlighted in a number of recent articles. When medications with low oesophageal absorption are administered effectively, absorption can be maximised and their absolute bioavailability increased [19].

Applications of Floating Microballoons

Floating microballoons were used as carriers to make sure the drugs were absorbed during the absorption window of the gastrointestinal mucosa. antibiotics, antifungals, antiviral medications, etc.

Reduced gastric irritation is the primary adverse effect due to administering nonsteroidal anti-inflammatory drugs (NSAIDs) through hollow microspheres with controlled release. Hollow microspheres are used to remove Helicobacter pylori from the stomach mucosa.

By increasing the drug's concentration in the stomach, hollow microspheres enhance gastric pharmacotherapy, which in turn suppresses H. pylori in the submucosal layer. Gastritis, oesophagitis, stomach ulcers, gastric and stomach ulcers, and other conditions can alleviate along with H. pylori suppression. One example is lansoprazole.

For drugs with poor bioavailability, floating microspheres are an excellent delivery strategy because of their low absorption in the oesophagus and small intestine. By promoting maximum absorption at the target site, these medications' bioavailability can be improved. Examples are riboflavin and furosemide.

When compared to oral controlled release formulations, floating microspheres have a longer residence duration, which is an advantage because they release the drugs gradually at the site of absorption [20].

Hollow microspheres containing non-steroidal anti-inflammatory drugs are an excellent controlled-release delivery system that mitigates the most common side effect, gastrointestinal distress. One example is the use of floating indomethacin microspheres, which are very helpful for rheumatic patients.

Floating microspheres are an excellent delivery system for drugs that are either poorly soluble or insoluble. As the solubility of a drug decreases, the amount of time it takes for the drug to dissolve

decreases as well; as a result, transit time becomes an important component in drug absorption. For drugs that aren't very soluble at alkaline pH, hollow microspheres can keep them in the stomach, where they won't be able to cause solubility to be the limiting step in release. Medications that are absorbed well by the stomach, such as verapamil hydrochloride, can benefit from positioned gastric release. The active agent's bioavailability will be enhanced due to the gastro-retentive floating microspheres' beneficial effect on the absorption profile [21].

CONCLUSION AND FUTURE POTENTIAL

GRDDS improves absorption-window drug bioavailability and control. High density, bioadhesive, swelling, magnetic, and floating systems were used in GRDDS. These methods release medication at optimal absorption sites with controlled release. Every medicine delivery strategy has pros and cons. GRDDS effectiveness depends on drug physicochemical qualities, GIT physiological activity, formulation methods, and drug-additive combinations. Several studies suggest that floating dosage forms may reduce plasma drug levels due to delayed stomach emptying. Low-bioavailability medicines with poor upper GIT absorption might be administered to maximise absorption and absolute bioavailability. Buoyant delivery can treat gastric and duodenal malignancies. The floating notion creates anti-reflux compositions. designing a Parkinson's medicine-controlled release mechanism. A small balloon can treat gastrointestinal ailments. Targeted drugs are given. Microballoons are utilised for more than GIT issues. There are various microballoon products, however research is continually being done to close the gap. Microballoon formulation is adequately discussed in this article.

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