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A Review on Multiple Unit Hallow Microspheres (Microballoons)

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ABSTRACT
The aim of writing this Microballoons review article is to accumulate recent literature with a particular emphasis on novel technical developments in the delivery system of floating drugs to achieve gastric retention. A possible technique for gastric retention promises to be micro balloons (Hollow microsphere/Floating microspheres). Microballoons are based on a non-effervescent systems comprising spherically shaped empty particles without a center core, preferably measuring 1-1000 micrometers in size. Gastro-retentive Micro balloons are structures of low density with ample buoyancy to float over gastric contents and for a long period of time stay in the stomach. The drug is released progressively at the target rate, leading to increased gastric retention and reduced variations in plasma drug concentration. Micro balloons can achieve improved therapeutic effects of short half-life drugs in order to increase patient compliance by decreasing dosing frequency. Because of buoyancy, gastric retention time is increased, increasing the absorption of drugs that solubilize only in the stomach. Optimized hollow microspheres, particularly in secure, targeted and successful in vivo delivery promises to be a possible approach to gastric retention, will be the central place in new drug delivery. In this article, the advantages, mechanism of micro balloons, methods of preparation, variables affecting micro balloons, the characterization, applications and A comprehensive list of medications that have been developed as floating microspheres are covered in detail.

KEYWORDS: Gastro retentive drug delivery, Floating drug delivery, Microballoons, Multiparticulate system, Non-effervescent system, Controlled release, Buoyancy

I. INTRODUCTION

Due to ease of administration, patient compliance and formulation stability, the oral route is considered as the most promising and preferred drug delivery route to achieve improved bioavailability and release of drugs from the system that should be predictable and reproducible, etc.[1,2]. In certain cases, the substantial variability of the physiology of the gastrointestinal tract and its transit period unfairly contributes to uncertain bioavailability and non-reproducible therapeutic results [3]. The controlled-release drug delivery system is capable of achieving benefits such as maintaining therapeutic drug concentration in the blood with a controlled release rate for an extended period of time; enhancing short-life drug activity; minimizing side effects; decreasing drug concentration fluctuations and dosing frequency; it optimized therapy and better patient compliances [4]. One prerequisite for the good output of drug delivery systems for oral controlled release is that the drug should be well absorbed via the gastrointestinal tract, preferably via passive diffusion [3].

A) Gastro Retentive Drug Delivery System

The gastro-retentive drug delivery system (GRDDS) has recently gained tremendous popularity in the oral drug delivery field. It is a commonly used solution to retaining the dosage type in the stomach for a prolonged period of time and slowly releasing the medication that can tackle many problems associated with traditional oral delivery, including poor bioavailability [5]. Gastro retentive dosage type will remain for several hours in the gastric region and thus significantly extend the duration of drug gastric residence. Prolonged gastric retention increases bioavailability and therapeutic effectiveness, decreases drug waste and enhances the solubility in a high pH setting of drugs that are less soluble. It is also effective for

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delivery to the stomach and proximal small intestine with local medications.

Gastro retentive Drug Delivery Systems Potential Drug Candidates:

- Narrow GI tract absorption window e.g., riboflavin and levodopa.
- Primarily ingested from the stomach and upper part of the GIT, e.g. calcium, chlordiazepoxide and cinnarazine supplements.
- Drugs that function locally in the stomach, for instance, antacids and misoprostol.
- Drugs that degrade in the colon, for example, metronidazole and ranitidine Hcl.
- Medications interacting with normal colonic bacteria, such as amoxicillin trihydrate
- A low density type of the DF that induces gastric fluid buoyancy.
- In the bottom of the stomach, high densitydosage form is maintained.
- Bioadhesion to mucosal stomach.
- Slowed gastrointestinal tract motility by concomitant administration of medications or prescription excipients.

Drug candidates that aren't appropriate for Gastro-retentive drug delivery systems include:

- Drugs with very small acid solubility, such as phenytoin, etc.
- Drugs suffering from gastric instability, such as erythromycin, etc.
- Drugs designed for selective colon release, such as 5-amino salicylic acid and corticosteroids, etc [6].

Approaches of Gastric Retention [7]

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B) Floating Drug Delivery System

Floating drug delivery systems (FDDS) or hydro-dynamically balanced systems have a lower bulk density than gastric fluids and thus stay floating in the stomach for a prolonged time without impacting the rate of gastric-emptying. The drug is released steadily at the optimal rate from the floating system after complete release; the residual system is eliminated from the stomach.This leads to an improvement in GRT and greater control over variations in the concentration of plasma drugs [8].

Floating Drug Delivery System classified Based on buoyancy mechanism

1. FDDS-Effervescent

As well as various effervescent compounds such as sodium bicarbonate, tartaric acid, and citric acid, there are matrix formulations of systems prepared using swelling polymers such as methylcellulose and chitosan. The matrices are made in such a way that carbon dioxide is released by the acidity of the gastric contents upon arrival in the stomach and is trapped in the gellified hydrocolloid. It induces an upward movement of the dosage type and retains its buoyancy. The dosage type floats on the chime due to a reduction in real gravity. [9]

I. Volatile liquid containing systems (Intragastric floating GRDDS)
II. Gas-generating Systems (Intra gastric single layer and bilayered floating tablets, Multiple unit type floating pills. [10]

2. FDDS Non-Effervescent

As a gel-forming or swellable cellulose type, non-effervescent floating dosage forms depend on hydrocolloids, polysaccharides, and matrix-forming polymers including polycarbonate, polyacrylate, polymethacrylate, and polystyrene. A easy method of thoroughly combining the drug and the gel-forming hydrocolloid is included in the formulation method. This dosage type swells when in contact with gastric fluids after oral administration and reaches a bulk density of < 1. The air trapped within the swollen matrix provides the dosage type with buoyancy. The swollen gel-like structure formed in this way serves as a reservoir and helps the gelatinous mass to sustainably release the drug. [11]

I. Hydro colloidal gel barrier systems
II. System of micro porous compartment
III. Beads of alginate and pectin
IV. Microsphere hollow (Micro balloons)

II. MICRO-BALLOONS

Microballoons are non-effervescent, gastro-retentive drug-delivery systems. In the strict sense, micro balloons (Hollow microsphere) are empty spherical-shape particles without a core. These microspheres are usually free-flowing powders composed of proteins or synthetic polymers that are preferably smaller than 200 micrometres in size. Micro balloons are considered one of the most favourable buoyant structures due to the central hollow space within the microsphere, with the unique advantages of multiple unit systems as well as better floating properties. At the target rate, the slow release and better floating properties of the drug depend primarily on the shape of the polymer, plasticizer and the solvents used in the preparation.Polymers such as polylactic acid, Eudragit® S and hydroxy propyl methyl cellulose, cellulose acetate are used in the formulation of hollow microspheres, and drug release can be modulated by optimising polymer concentration and optimising polymer release and polymer-plasticizer ratio optimization. [10]

Advantages of Micro balloons

1. It improves the bioavailability.
2. Sustains the delivery of drugs
3. Decreases dosing frequency and thereby increases patient compliance.
4. Targeted treatment is used in the upper gastrointestinal tract for local ailments.
5. Minimize drug fluctuations.
6. Reduce the colon's harmful behaviour.
7. Hollow microspheres are used to reduce material density, while buoyancy increases gastric retention time.
8. Minimize the amount of gastric irritation caused by acidic drugs.
9. The biological half-life of the drug is shortened when vigorous bowel activity occurs during diarrhoea. The floating microspheres float in the gastric content in that state and increase absorption.
10. As such microspheres are superior to single unit floating dosage types, they release drugs uniformly and there is no chance of dose dumping.
11. Improved therapeutic results can be achieved with short half-life drug. [4,12]

Limitations of Micro balloons

a) For drug delivery, these devices need a high amount of fluid in the stomach to float and function efficiently.

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b) Not suitable for medicines with GIT solubility or stability issues.
c) Drugs such as nifedipine, which is well absorbed in the entire GIT and undergoes first pass metabolism, may not be advisable.
d) It is also not necessary to consider medications that irritate the gastric mucosa.
e) Drug substances which are unstable in the stomach's acidic environment are not suitable candidates for incorporation into the systems.
f) A full glass of water should be administered in the dosage form with (200-250 ml).
g)These systems are not beneficial for certain medications that are absorbed in the gastrointestinal tract relative to traditional dosage types. [2]

III MECHANISM OF MICROBALLOONS

Micro balloons are low-density systems with enough buoyancy to float above gastric fluid and stay in the stomach for a long time. The drug is released slowly and at the optimum rate as the system floats over gastric fluid, resulting in greater gastric retention and lower variations in plasma drug concentration. As micro balloons come into contact with gastric fluid, the gel forms and the polymers hydrate, forming a colloidal gel barrier that regulates the rate of fluid penetration and drug release into the device. When the outer surface of the dosage type dissolves, the gel layer is protected by the hydration of the underlying hydrocolloid layer.

The swollen polymer traps oxygen, which lowers the density of the gastric fluid and gives the microspheres buoyancy. However, in order to achieve proper buoyancy, a small amount of gastric content was needed.The latest developments are hollow microspheres (micro balloons) of acrylic resins, eudragite, hypromellose, polyethylene oxide, cellulose acetate, floatable polystyrene shells, floating polycarbonate balloons and floating gelucire granules.[4,13]

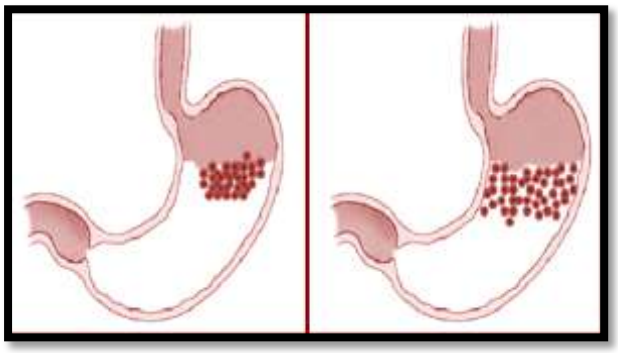

Fig1: Schematic representation of floating microspheres

Mechanism of the release of drugs from the microspheres.
Multi-particulate drug release can take place in a variety of ways: -
a)Diffusion Water diffuses into the interior of the particle as a result of interaction with aqueous fluids in the gastrointestinal tract (GIT). The drug solutions are dissolving and moving to the exterior through the release coat.
b)Erosion Certain coatings can be engineered to gradually erode over time, releasing the material trapped in the particle.
c)Osmosis Inside the particle's interior, an osmotic pressure may be created in order to allow water to enter under the right conditions. The drug is forced out of the particle into the exterior through the coating. [14,15]

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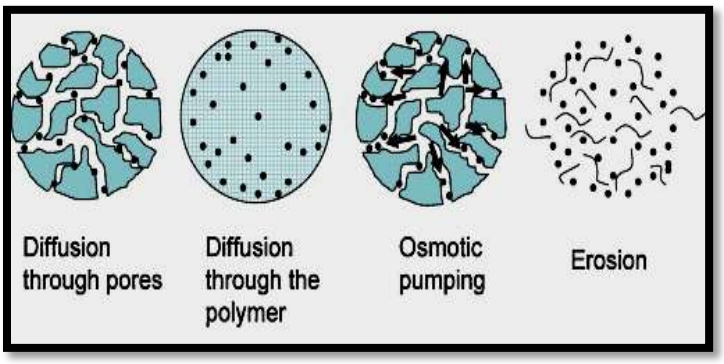

Fig2: True release mechanism

IV PREPARATION OF MICROBALLOONS

(a) Method of solent evaporation: There are essentially two systems for emulsion solvent evaporation, namely the oil-in-water (o/w) and water-in-oil (w/o) forms.

i) Technique of Oil-In-Water Emulsion Solvent Evaporation

In an organic solvent, the polymer is dissolved and the drug is either dissolved or dispersed in the polymer solution. The drug-containing solution is then emulsified into an aqueous phase containing an appropriate additive (surfactants/polymer) to form a water emulsion oil. By continuous stirring, the organic solvent is either evaporated by raising the temperature under pressureor, after the creation of a stable emulsion. The removal of solvent contributes to the precipitation of polymers at the droplet oil/water interface, creating cavities and thereby rendering them hollow to impart the floating properties (Fig3). Cellulose acetate, chitosan, eudragite, acrycoat, methocil, polyacrylates, polyvinyl acetate, carbopol, agar, polyethylene oxide and polycarbonate are the polymers studied for the production of such systems.[16,17]

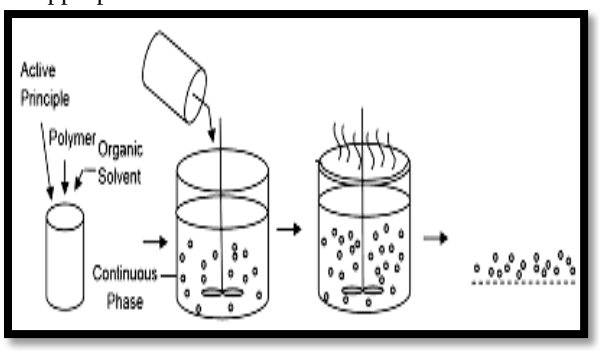

Fig3: Oil in Water evaporation

ii) Technique of Oil-in-Oil Emulsification Solvent Evaporation

This oil-in-oil method of emulsification (sometimes referred to as water-in-oil) is also known as non-aqueous emulsification solvent evaporation. Drugs and polymers are codissolved in polar solvents such as ethanol, dichloromethane, acetonitrile, and others at room temperature with vigorous agitation to form uniform drug-polymer dispersion. In the presence of oil-soluble surfactants such as Span, this solution is slowly poured into a dispersion medium made up of light/heavy liquid paraffin. The system is stirred to ensure maximum solvent evaporation using an overhead propeller agitator at 500 revolutions per minute (rpm) and room temperature for a period of 2-3 hours. The liquid paraffin is decanted and the microparticles are separated by filtration with Whatman filter paper, washed three times with n-hexane, air-dried for 24 hours and then placed in desiccators.

Span 60, a surfactant which is non ionic, is widely used. Span 60 has a value of HLB 4.3 and functions as a droplet stabilizer and prevents

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droplet coalescence by localizing the dispersed phase and dispersion medium at the interface. [2]

(b) Emulsion Solvent Diffusion Method:

In the emulsion solvent diffusion process, the affinity between the material and the organic solvent is greater than the affinity between the organic solvent and the aqueous solvent. Even though the organic solvent is miscible in the aqueous solvent that forms the emulsion droplets, the substance is dissolved in it and the solution is dispersed. The organic solvent gradually diffuses from the emulsion droplets into the surrounding aqueous phase, while the aqueous phase diffuses into the droplets through which the substance crystallises. [18]

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(c) Solvent Diffusion-Evaporation Technique:

This approach requires a minor alteration of both the method of emulsion solvent evaporation and the method of emulsion solvent diffusion. In the ethanol solution, drugs, polymers and 0.1 percent of surfactants such as PEG are mixed with dichloromethane at room temperature (1:1). Slowly apply this solution to 80 ml of polyvinyl alcohol as an emulsifier of 0.46% w/w this is extracted and then filtered for 1 hour for organic solution evaporation using a propeller agitator (Fig4). The best formulation is chosen based on the optimised results of various process variables such as polymer ratio, drug: polymer ratio, stirring speed, and emulsifier concentration. [4, 7]

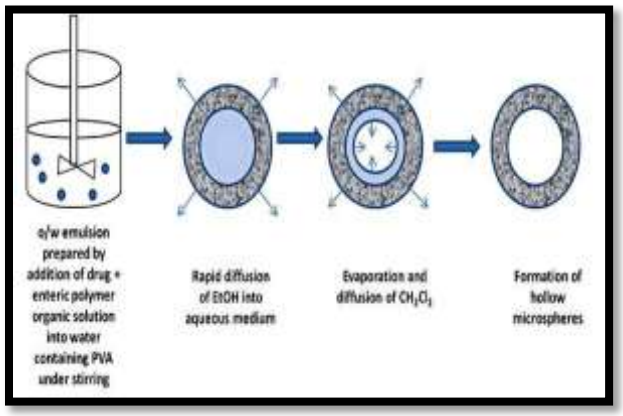

Fig4: Solvent diffusion-evaporation method

(d) Ionotropic Gelation Method

The tendency of poly electrolytes to cross link in the presence of counter ions to form beads is referred to as ionotropic gelation. Since the use of alginates, gellan gum, chitosan, and carboxymethyl cellulose for encapsulating drugs and even cells, the ionotropic gelation technique has been widely used for this function. Natural poly electrolytes, despite having coating properties on the drug core, act as release rate retardants due to the presence of anions in their chemical structure. By combining with polyvalent cations, these anions form meshwork structures that cause gelation by binding primarily to anion blocks. The hydrogel beads are created by dropping a drug-loaded polymeric solution into a polyvalent cation aqueous solution (Fig5). [19]

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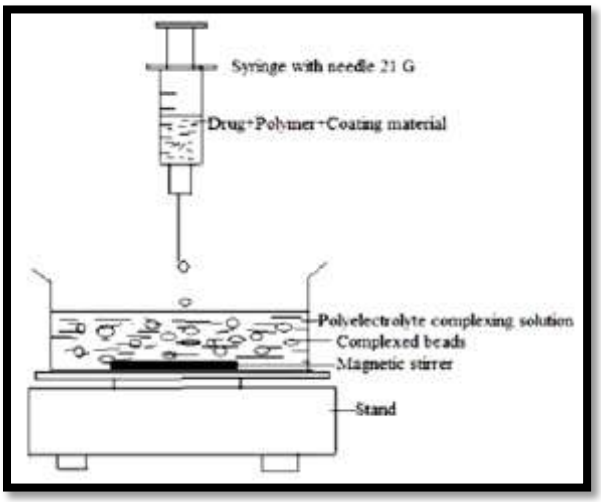

Fig5: Ionotropic Gelation technique

(e) Spray drying

The polymer is first dissolved in a volatile organic solvent including dichloromethane or acetone. The drug in solid form is then distributed in the polymer solution through high-speed homogenization. This dispersion is then atomized in a stream of hot air. The atomization process produces small droplets or fine mists from which the solvent evaporates quickly, resulting in the creation of microspheres with sizes ranging from 1 to 100 micrometres. Micro particles are separated from hot air using a cyclone separator, while solvent traces are removed using vacuum drying (Fig6). One of the system's most significant advantages is its ability to operate under aseptic conditions. This method produces porous micro particles quickly. [20]

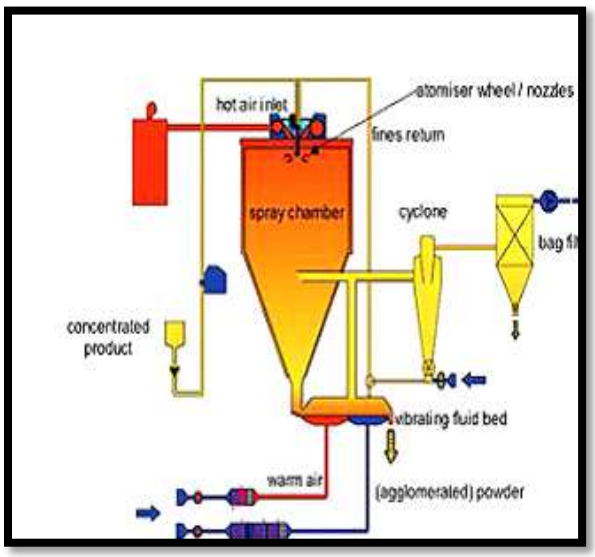

Fig6: Spray drying method for microballoons

V FACTORS AFFECTING PHYSICO-CHEMICAL PROPERTIES OF MICROBALLOONS

a) Stirring rate: The size of the microspheres is proportional to the rate at which they are stirred.Increased agitation results in a reduction in microsphere size, but the difference is statistically insignificant. Within the study set, the majority of the polymers are incapable of being broken down into fine droplets.

b) Preparation temperature: The drug and polymer solution are poured at different

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temperatures such as 20, 30, 40, and 50 degrees Celsius. At 20 or 30 degrees Celsius, the surface porosity of the microspheres increases. The size of the particle shrinks as the temperature rises. The emulsion viscosity is decreased at higher temperatures as the mixing input power is increased, making it much easier to break down the emulsion.

c) Plasticizers: Plasticizers are added to the material's walls to give it elasticity and flexibility. The addition of plasticizers prevents bursting under pressure or brittleness. The amount of drug released increases significantly as the plasticizer concentration rises.

d) Solvent ratio: Irregularly shaped microspheres were created by bridging a small volume of solvent, while bridging a large volume of liquid prevents emulsion droplets from solidifying. The amount of solvent must be carefully regulated. The morphology of the microspheres is influenced by the ratio of two solvents. The ratio must be optimised to produce spherical microspheres.

e) Polymer concentration and viscosity: Smaller microballoons were produced at lower polymer concentrations, exposing the drug to a greater surface region, resulting in faster drug release.

f) Emulsifier concentration: As the surfactant concentration decreases from 1% to 0.25 percent, the particle size and distribution increase. Emulsifiers are important because they reduce interfacial tension between dispersed droplets and the continuous phase, as well as prevent droplets from colliding and coalescence. [21,22]

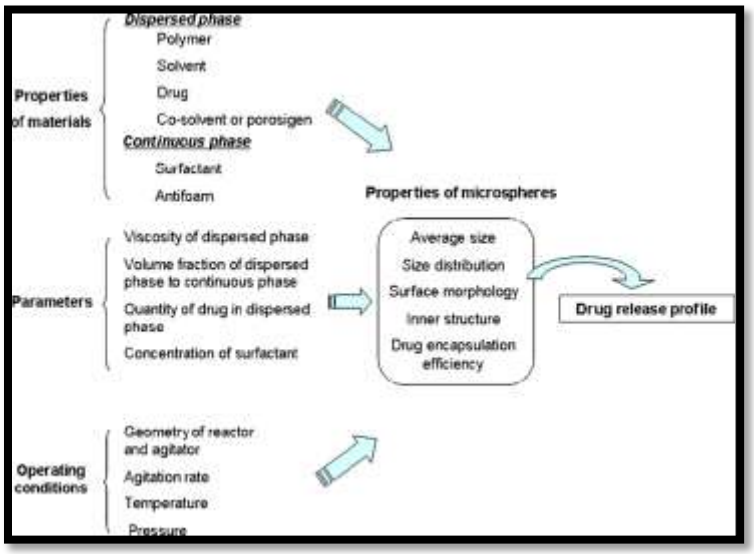

Fig7. Schema of the factors influencing the properties of microspheres.

VI. CHARACTERIZATION / EVALUATION OF FLOATING MICROSPHERES

1)Particle size [3]

Particle size is measured with an optical microscope, and mean particle size is calculated with a calibrated ocular micrometre by measuring 100-200 particles. Different sizes of microspheres and their distribution in each batch are calculated by sieving in a mechanical shaker with a nest of regular sieves (ASTM) and a 15-minute shaking time. The mean particle size of microspheres is determined using the formula below, which estimates the distribution of particle size.

Mean particlesize=∑(meanparticle sizeof the fraction× weight fraction)/∑(weight fraction)

2)Bulk density [18]

The bulk density is calculated by dividing the powder mass by the bulk volume. Weighed to a precision of 10 gm. A 25 ml measuring cylinder was used to hold the granule sample. The volume occupied by the granules was measured without disturbing the cylinder, and the bulk density was calculated using the equation (values expressed in gm/cm3).

$$\text{Bulk density} = \frac{\text{Weightofsample}}{\text{volumeofsample}}$$

3) Tapped density

Tapped densities can be calculated using the tapping process. The volume of weighted amounts

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of microspheres was measured after 100 and 1000 taps using tapped density apparatus.

$$\text{Tapped density} = \frac{\text{weightofsample}}{\text{tappedvolume}}$$

4) Compressibility Index and Hausner Ratio [18,23]

From the values of bulk density and tapped density, the compressibility index and hausner ratio were calculated using the following formulas:

$$\text{Compressibility index} = \frac{\text{tappeddensity} - \text{bulkdensity}}{\text{tappeddensity}} \times 100$$

$$\text{Hausner Ratio} = \frac{\text{Tappeddensity}}{\text{Bulkdensity}}$$

Carr's index	Type of flow
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
>40	Extremely poor

Table 1:Realtionship between Carr's index and type of flow

5) Scanning electron microscopy analysis: [24]

SEM analysis: The shape and surface morphology of microsphere samples were observed under SEM. Microspheres were clustered on to double-sided carbon dust, which was mounted on to sample carrier (9 aluminium stubs with double adhesive tape) in the shape of a cylinder with a weight of 5 mm and a diameter of 10 mm. and were sputter coated to a thickness of 50 nm with AU-pd (Gold Platinum) mixture under vacuum (9100 m torr). A 5-15 kV electron beam was used to photograph the samples. For surface topography, appropriate magnification microsphotographs were obtained.

6) Percentage Yield [25]

The percentage yield of floating microspheres was calculated by dividing the actual product weight by the total quantity of all non-volatile components used in their preparation.

% yield = (actual weight of product/total weight of drug and Excipients) ×100

7) Angle of Repose [26]

The funnel method was used to measure the powder blend's resting angle. The right weighted powder blend was placed in the funnel. The funnel's height was adjusted so that the funnel's tip just touched the powder mixture's apex.

The powdered mixture was permitted to flow freely through the funnel to the surface.The diameter of the powder cone was determined and, using the following equation, the angle of repose was estimated.

$\tan \theta = h/r$

Therefore

$$\theta = \tan^{-1} h/r$$

Where, θ = angle of repose,
h = height of the pile
r = radius of the pile.

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Angle of Repose	Flowability
< 25	Excellent
25-30	Good
30-40	fair
> 40	Very poor

Table 2: Relationship between angle of repose (˚) and flowability

8) Drug entrapment efficiency (DEE)[25]

The amount of drug trapped was calculated by crushing the microspheres and extracting them with aliquots of 0.1N HCl. To make up the volume 0.1N Hcl was used to pass the extract to a volumetric 100 ml flask. A spectrophotometer was used to calculate the absorbance of the solution in comparison to a suitable blank.The quantity of drug trapped in the microspheres was determined by thefollowing formula:

DEE = (amount of drug actually present/theoretical drug load expected) × 100

9) Swelling studies [4]

Swelling experiments are used to determine the molecular parameters of swollen polymers. Dissolution tools, optical microscopy, and other specialised methods, such as H1NMR imaging, confocal laser scanning microscopy (CLSM), cryogenic electron scanning microscopy (Cryo-SEM), light scattering imaging (LSI), and dissolution apparatus (USP dissolution apparatus USP-24) lab India disso 2000) others, are used to assess swelling .Swelling studies are determined in accordance with the following formula.

$$\text{Swelling ratio} = \frac{\text{weig ht of wet formulations}}{\text{weightofformulation}}$$

10) In-vitro buoyancy [27]

In 900 ml of 0.1N HCl, a suitable amount of hollow/empty microspheres is added. In a dissolution apparatus, the mixture is stirred for 8-10 hours at 100 rpm. After 8 to 10 hours, pipette and filter the layers of buoyant microspheres apart. Filtration is used to remove particles that are suspended in the sinking particulate layer. Both types of particles (buoyant and settled microspheres) are dried in a desiccator until they achieve a constant weight. In vitro buoyancy is determined by the weight ratio of floating microspheres to the number of floating and sinking microspheres, as well as the percentages of empty/hollow microspheres.

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

Where Wf and Ws are the weight of floating and settled microsphere respectively

11) In-vitro drug release studies [4]

The release rate of hollow microspheres is determined using a United States Pharmacopeia (USP) XXIII basket type dissolution apparatus. The basket is filled with a weighed quantity of hollow microspheres (filled with a hard gelatin capsule) equal to the drug's dose, as well as the dissolution rate apparatus containing the dissolution medium. The dissolution fluid's temperature is maintained at 37±1 °C, and the rotation speed is maintained at a precise rpm. Perfect sink conditions are preserved throughout the drug release analysis. At each time interval, a few ml (5 ml) of samples are taken and analysed using liquid chromatography/mass spectroscopy to determine the concentration of microballoons in the dissolution medium. By adding 5 ml of fresh dissolution fluid for each withdrawal, the initial volume of the dissolution fluid is retained. Both tests are carried out three times.

12) Data analysis of release studies [10]

Using PCP Disso v3 software, five kinetic models are used to find the best fit equation for the in vitro release results: zero order (Equation 1), first order (Equation 2), Higuchi matrix (Equation 3), Peppas-Korsmeyer (Equation 4) and Hixon-Crowell (Equation 5)

13) In vivo studies [28]

Floating activity in vivo Healthy albino rats weighing 500–600 g received an optimised formulation and were tracked using a modified radiological system [1]. The Shri Ram Institute of Technology Pharmacy Institutional Animal Ethics Committee in Jabalpur, Madhya Pradesh, approved the research (Protocol No: SRITP/IAEC/2014/01). Individual animals were housed in polypropylene cages and held under normal conditions (12-hour light/12-hour dark cycle; 25–30 C). The animals were fasted for 12 hours and X-rays were taken to

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ensure that there was no radio-opaque material in the stomach. During the study, the animals were not allowed to eat, but they were given unlimited access to water. The radiopaque microspheres were made by mixing 500 mg of barium sulphate into a polymer solution, and the optimised formulations were made in the same way. To monitor the floating, activity of microspheres X-ray images of the gastric region (Siregraph-B, Siemens, Karlsruhe, Germany) were taken at various time intervals.

VII APPLICATIONS OF FLOATING MICROSPHERES

- Floating microspheres are a very good option for the delivery of drugs with poor bioavailability due to insufficient absorption in the upper GIT. These systems efficiently improve drug absorption and increase the bioavailability of multiple drugs. For example, furosemide, riboflavine, and others.
- Antiviral, antifungal, and antibiotic agents (sulphonamides, quinolones, penicillins, cephalosporins, aminoglycosides, and tetracyclines) are only extracted from specific parts of the gastrointestinal mucosa. Drugs with absorption windows could be carried by the floating microspheres.
- Gastro retentive floating microspheres are very helpful in reducing major adverse effects of gastric irritation; for example, floating microspheres of nonsteroidal anti-inflammatory drugs, such as Indomethacin, are beneficial for rheumatoid arthritis patients.
- These systems are particularly beneficial for medications that must be absorbed from the stomach or the proximal part of the small intestine, such as riboflavin, frusemide, and misoprostol. The desired therapeutic level may be achieved by slowing the delivery of misoprostol to the stomach and reducing drug waste.
- These microspheres systems provide sustained drug release behavior and release the drug over a prolonged period of time.Tranilast hollow microspheres are produced as a floating drug delivery device that is managed.
- Prednisolone, lansoprazole, celecoxib, piroxicam, theophylline, diltiazem, verapamil, riboflavin, aspirin, griseofulvin, ibuprofen, and terfenadine are among the drugs recently found to be entrapped in hollow microspheres.

There are several others significant applications of FDDS as summarized below:

Sustained Drug Delivery

HBS systems can stay in the stomach for longer periods of time, allowing the medication to be released over a longer period of time. The problem of a short gastric residence time with an oral Controled Release formulation can be solved with these systems. Since the bulk density of such systems is less than one, they can float on the gastric contents. Since these structures are relatively large in size, passing from the pyloric opening is prohibited.

Delivery of Site-Specific Drugs

These systems are particularly useful for drugs that are directly absorbed from the stomach or the proximal part of the small intestine ex. Furosemide &riboflavin.

Enhancement for Absorption

Low bioavailability drugs can be formulated as floating drug delivery systems to improve absorption by site-specific absorption from the upper gastrointestinal tract[6].

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Table 3: Marketed Preparations of Floating Drug Delivery Systems

Sl no	Drugs	Product	Reference
1	Levodopa and Benserzide	Madopar	29]
2	Diazepam	Valrelease	[30]
3	Aluminum magnesium antacid	Topalkan	[31]
4	Antacid	Almagate Flot-Coat	[32]
5	Alginic acid and sodium bicarbonate	Liquid gavison	[33]

Sl no.	DRUG	Reference
1	Aspirin, griseofulvin and p-nitroaniline	[34]
2	Ibuprofen	[35]
3	Tranilast	[36]
4	Ketoprofen	[37]
5	Verapamil, Verapamil HCl	[38, 39,1]
6	Repaglinide	[40]
7	Cimetidine	[41]
8	Orlistat	[42]
9	Rosiglitazone	[43]
10	Nitrendipine	[44]

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11	Aceclofenac	[45]
12	Acyclovir	[46,47]
13	Riboflavin	[36,48]
14	Acetohexamic acid	[49]
15	Ranitidine HCl	[50]

Table 4: List of the drugs formulated as a floating microspheres

CONCLUSION

In the Gastrointestinal tract, drug absorption is a highly variable mechanism, and increasing the time it takes for drugs to be absorbed by prolonging the dosage form's gastric retention. As gastro retentive dosage forms, floating microspheres precisely regulate the release rate of the target drug to a specific site and have a huge impact on health care. Microballoons have a high proclivity for causing gastroretention and are an efficient way to increase bioavailability and monitor the release of a variety of medicines. The floating micro-balloons are promising candidates for the development of GRDDS with therapeutic benefits. These multiparticulate systems also provide enormous opportunities in the design of new controlled and delayed release oral formulations, broadening the frontier of future pharmaceutical development.

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