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HOLLOW MICROSPHERE AS A DRUG CARRIER: - A REVIEW OF CLASSIFICATION AND PREPARATION TECHNIQUE WITH THEIR APPLICATION

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ABSTRACT

The aim of writing this review on microballoons is to pile up the contemporary literature with a main focus on the novel technological advancements in the floating drug delivery system to achieve gastric retention. Microballoons (Hollow microsphere) assurance to be a potential approach for gastric retention. Microballoons drug-delivery systems are the concept of non-effervescent system accommodating unoccupied particles of spherical shape without core, preferably having a size less than 200 micrometre. the drugs having site-specific absorption for those microballon drug delivery system proven a better significance in controlling the release rate. The floating microballoons presented gastroretentive controlled release delivery of enhancing the bioavailability and promises to be a possible approach for gastric retention. Optimized hollow microspheres will locate the central place in novel drug delivery, especially in safe, targeted, and effective in vivo delivery conveyance to be a possible methodology for gastric retention. They are gastroretentive drug-delivery systems, which give controlled discharge properties. This review focus on limitations, methods used for preparation of hollow microsphere, applications of the hollow microsphere, polymers utilized in hollow microspheres, characterizations of microballoons, and formulation with different assessment and marketed products are covered in detail.

KEYWORDS: Microballoons, Gastroretentive, Buoyancy, absorption, Floating drug delivery system (FDDS) gstric residence time.

INTRODUCTION

An oral dosage form consisting of a tablet, capsule provides a calculated drug amount inside the circulation of the body system. Where some of them don't discharge their medication at a constant rate for a delayed timeframe. The drug delivery in the Controlled-release framework releases its drug at a previously known rate either they are systemic or topical or locally for the calculated timeframe and optimize the corrective activity of the drug because the drug release is in a controlled manner into the system with less dose & reduce frequency dose Controlled release.[1,2,3]

This drug delivery framework which releases the drug in a controlled manner is consistent with accomplishing the benefits like this continuation of a therapeutic amount of drug percentage in serum stays for longer timeframe at a controlled release rate. for short half-life drugs the refinement in the activity of duration, depletion in side effects, reduction in the fluctuation of drug concentration, and recurrence of dosing. it helps for patient compliance and in therapy.[4-7]

Floating drug delivery system

The low-density system like the Floating drug delivery system or hydrodynamically controlled framework has enough buoyancy in the stomach for, explicit timeframe. while the gastric content allows the system to float in it. the dose has been releasing its drug from the stomach slowly for the required rate. the remaining system is emptied from the abdomen at the point when the release of the drug is completed. This shows a better control on fluctuation, increment in GRT in plasma drug concentration. for accurate achievements of the buoyancy, a minimal gastric content expected, to maintain a dosage form buoy over the meal and quiet floating force (F) is also needed. There are numerous buoyant systems are available those are based on granules, powder, capsule, tablet, laminated film, and hollow microsphere enlisted example of various dosage formulated as a different form of floating drug delivery system (FDDS).[8-10]

Advantages of floating drug delivery system

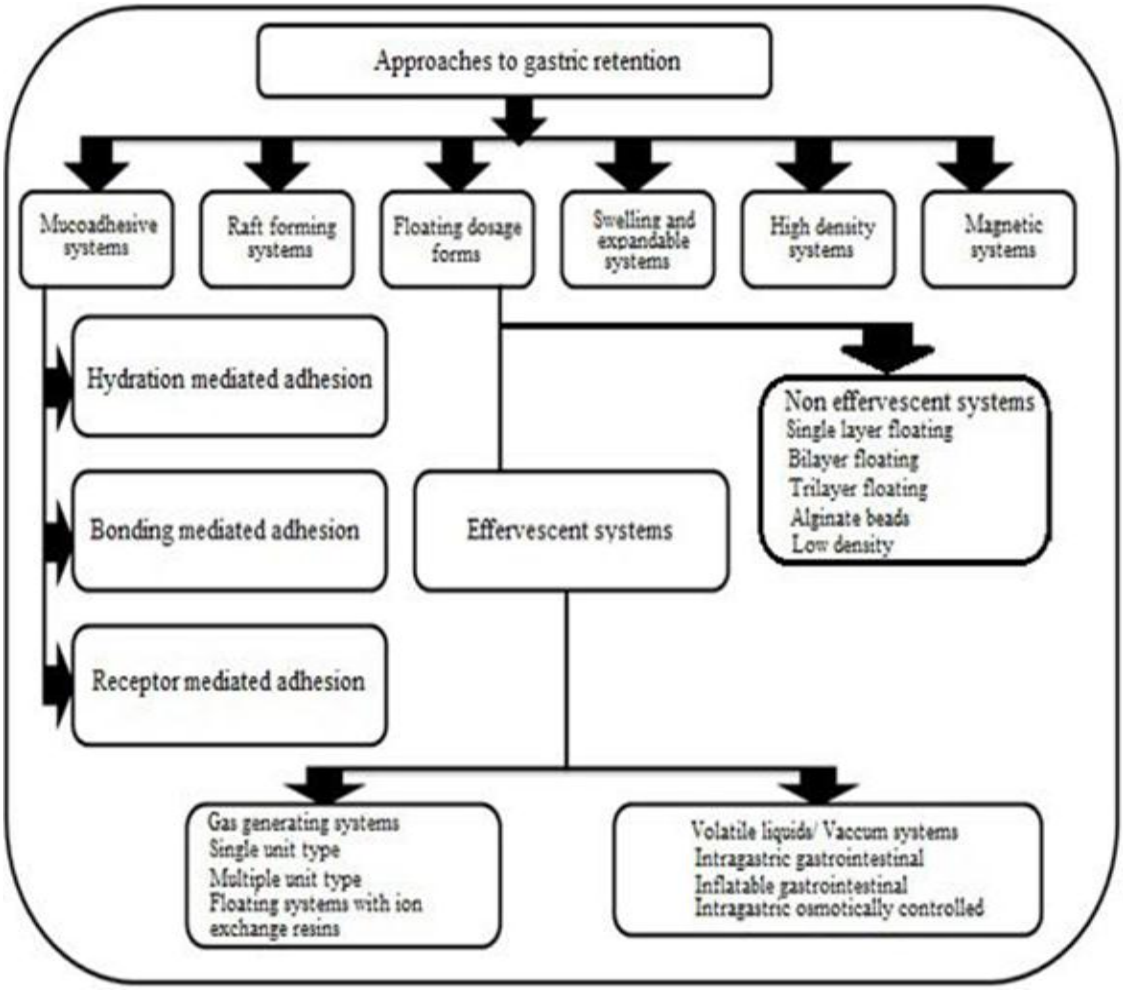
There are several advantages to this medication delivery system with gastric retentive behavior. Some of these include:

1. A basic and conventional technique for formulation.
2. Site-specific drug delivery.
3. Controlled delivery of drugs.

4. Conveyance of drugs for residual action at a specific site in the stomach.
5. Improved drug assimilation with expended GRT and excess duration of contact of the dosage regimen at its target site.
6. Limiting irritation of GIT mucosa by the drugs with a moderate release rate. Acidic drug substances like anti-inflammatory medicine influence irritation to gastric mucosa as it comes in contact. Consequently, HBS formulation would be advantageous in the intake of aspirin and some comparative drugs. The dissolution of the drug in the gastric fluid happens because of the intake of longer released floating dosage forms like tablets or capsules. Before they are getting absorbed in the small intestine first, they have to dissolve in the gastric juice. Consequently, it could be expected that floating dosage forms will be fully absorbed, even at the basic pH of the intestine & remains in the solution form.
7. When at a short transit time, there would be vigorous intestinal movement, it may bring about a particular kind of loose bowel hence poor absorption could be expected. When such conditions appear, it is important to keep the drug in a buoy situation in the body for superior efficacy.
8. In treating gastroesophageal reflux disorders (GERD). The administration would be easy with higher patient comfort. The floating drug delivery framework also conveys specific disadvantages that limit its applicability.[11-13]

Disadvantages of floating drug delivery system

1. The main significant inconvenience of a floating delivery system is due to the necessity of an adequate level of gastric fluids to float without a sink. However, we can easily overcome this problem by coating with bio adhesive polymers it has the advantage of easily stick to the gastric mucosa.
2. The desirable candidate drugs are those that get absorbed throughout GIT with significant first-pass metabolism.
3. Certain drugs may cause bothering to gastric mucosal linings those present in the floating system.
4. The emptying rate of floating systems may occur at random and highly dependent on their measurements. consequently, patients cannot take dosage before going to bed.[14-17]



Classification of floating drug delivery systems

A. Effervescent system floating drug delivery system

These are made up of network type furthermore an expendable polymer like methylcellulose and chitosan along with buoyant compounds. These should be developed in such a particular path as once it interacts with gastric juice; co2 gets liberated with entrapment in expendable hydrocolloid to provide buoyancy for dosage form. The premise of the delivery system is on a swellable asymmetric triple-layer tablet approach design.

I. Gas generating systems

This system is based on the phenomenon after the arrival of co2 after the exposure with the gastric fluids. After the entrance in the stomach, co2 is liberated because it interacts with acidic gastric content which gets entrapped in the gel-based hydrocolloid. it maintains its buoyancy because of the upward motion of the dosage form. At the end, it decreases in specific gravity of the dosage form and maintains buoyancy. The co2 segments are assorted within the tablet matrix as single or double layered that produce gas and generating mechanisms in the hydrocolloid layer, in the other layer provide continue discharge.

II. Volatile liquid containing systems (Osmotically controlled drug delivery system)

This contains a device that encompasses of a hollow deformable unit in convertible collapsed form. The device would be attached to its deformable unit divided internally in between the first and second chambers which is separated by an impermeable, pressure-sensitive movable unit.

The active drug is placed in the principal chamber while at the physiological temperature second volatile liquid vaporized to deliver a gas empowering the drug reservoir to coast. At the end drug get eliminated from the stomach with bio erodible plug that allowed the vapor to escape.

B. Non-effervescent FDDS

Non-Effervescent Floating Drug Delivery Systems are made up of polysaccharide alongside matrix-forming polymers which comprise a gel-forming (or) swellable cellulose kind of hydrocolloids. The standard formulation contains the process where the drug is blended with gel framing hydrocolloids when it comes in contact with gastric fluid it swells and keeps up the integrity of shape and a bulk density barrier the integrity of shape and a bulk density barrier.

I. Colloidal gel barrier systems (Hydrodynamic balanced systems)

In this system, the drug that reaches its absorption site in the solution form by dragging out gastric retention time and augment the amount. Mostly this system remains buoyant on the stomach content because that contains itself gel-framing hydrocolloids. This type of systems incorporates one or more gel-forming cellulose type hydrocolloid e.g. (HPMC), polysaccharides and matrix-forming polymers. When it comes in contact with GI fluid one or more gel-forming cellulose-type hydrocolloid generate which hydrate to encompassing.

II. Microporous compartment systems

This innovation follows the strategy that contains the drug reservoir inside a microporous compartment alongside pores at the top as well as bottom walls. The direct contact of the gastric surface and the undissolved drug is prevented by the peripheral wall of the drug supply compartment. The delivery system that floats over the gastric content is made out of entrapped air called the floatation chamber which causes the delivery system to float over the gastric content. The dissolved drug that transports continuous across the intestine for absorption where Gastric fluid enters through the gap to prevents their existence.

III. Floating Microspheres/Micro balloons

Hollow microspheres also are known as micro balloons and are the most proficient buoyant system. These contain central hollow space inside the microsphere and contain the drug at the outer surface. Hollow microspheres are loaded with a drug on their external polymer shelf are fabricated by a different method.

IV. Alginate beads/Floating beads

Floating dosage forms are created or prepared from calcium alginate spherical normally about the size 2.5 mm in diameter. These can be prefabricated by adding cacl2 to the solution of sodium alginate, which bring the precipitate of calcium alginate, and further separated from the solution and freeze-dried at 400 °C for 24 h, which leads to the form of a porous system. This created system would buoyancy for over 12 h and these floating beads provide a long drawn out time of more than 5.5 h.

(C) Raft-forming systems

These systems are in much consideration for gastro infection and disorders for the utilization of antacid and other drug delivery. When the drug comes in contact with gastric liquid, a viscous cohesive gel formed with co2 bubbles because of gel framing solution swellable nature subsequently facilitates releases drug gradually in the stomach.[19-25]

Hollow microsphere / micro-balloon

Microballoon is gastro retentive drug delivery system that follows the category of non-effervescent technique. Micro balloons are globular shaped vacant particles in the absence of any core. These microspheres are, preferably having a size not more than 200 micrometres and having a property of free-flowing powder those are composed of protein or synthetic polymers.[26]

Due to central hollow space inside the microsphere, the micro balloons deal with the nearly all admiring buoyant system with a unique advantage of numerous unit systems and higher standard floating property. In the preparation of micro balloon, it involves some of these novel techniques include simple solvent evaporation method, solvent diffusion technique, phase separation coacervation technique, solvent evaporation-diffusion strategy, spray drying technique, spray congealing technique. The polymer's type, plasticizers, and solvent are the main component that affects the speed of drug at the desired rate and properties of buoy employed for the preparation. Several polymers like polylactic acid, cellulose acetate, etc

were utilized in the formation of microballoon. By varying polymer concentration & the polymer plasticizer proportion, the arrival of the drug can be modulated.[27-30]

By using some of the methods like the evaporation of solvent phase or solvent evaporation/diffusion method the hollow inner side core of microballoon, where the drug is loaded in their external outer shell could be created. The acrylic polymer mixture is solvated in ethanol/dichloromethane mixture and an unsettled arrangement of PVA that is previously thermally controlled at 30-degree calicoes mixed in the acrylic polymer solution. When enhancement of the temperature is done under the pressure condition by continuous stirring and previously prepared stable emulsion formed by evaporating the organic solvent from the emulsion.[31]

Material used for preparation of micro balloon

Drug– There is a specific criterion that the drug should have the properties of, limited therapeutic window in GIT. It should be absorbed from the stomach & upper piece of GIT and must locally act in the stomach & corrupt in the colon by disturbing normal colonic bacteria ex aspirin.[34]

1. Polymer – These play a vital role in this delivery system because they provide the controlled release at a constant rate. Polymers used micro balloon preparation are methocil, eudragit, agar, PVA, Cellulose acetate, chitosan, acrylic gum.[35-37]

2. Solvents – Polar and bipolar there is two types of solvents are available but, in this system, great volatile properties are necessary. So that the solvent could be effectively tearing out from the emulsion by leaving the microsphere hollow from inside ex- ethanol, acetone, isopropyl alcohol, DCM (dichloromethane.[38]

3. Processing medium - This is important to solidify the beads that contain drug-polymer emulsion when drug polymer's combined solution drop included in it. solution the former should not interact by the processing medium. The mostly used processing medium is paraffin (liquid form), H2O, PVA

4. Surfactants- they are used to enhance the tension of the surface or used to stabilize or emulsifying. But in this preparation, they are used to form the microballoon and to harden the microsphere ex – tween 80, span 80, SLS.

5. Cross-linking agents- cross-linking agent such as formaldehyde chemical cross-linking of microsphere can be accomplished. The drug do not have any collaboration with cross-linking agents this should also be remembered.[39]

6. Hardening agent – without a hardening agent the microsphere cannot form it with soluble in the emulsion. these assist with solidifying the microsphere framed in the processing medium ex – n-hexane.[40]

Mechanism of action

Microballons are a low-density system and have the property to buoy because of buoyancy the microballons float over gastric fluid & stay buoy in the abdomen for a longer period of timeframe. At the point When the microballoons float above the gastric environment the drug release gradually at the needed rate. Which reduces variation in plasma drug concentration and increases gastric retention. When micro balloon swells to form the gel and polymer swell to form the colloidal gel obstruction because it comes in contact with the gastric juice. it helps in adjusting the rate of liquid infiltration and the drug release continuously at a predetermined rate. a gel layer is formed with the help of hydration of the adjacent hydrocolloid layer As soon as the outer surface of the dose dissolve. The air caused density less than the gastric fluid and provides the quality to the microsphere of buoyancy. So, this is the reason why a minimal gastric liquid is essential for the achievement of proper buoyancy.[41-43]

Factors affecting gastric retention

Density- The dose Density ought to be not exactly the gastric substance (1.004gm/ml).

Size- More than 7.5 mm diameter of the Dosage form is resulted an expended GRT, comparatively with a width of 9.9 mm.

Fed or unfed state- The MMC also called migrating myoelectric complexes that happen after every 1.5 to 2 hours the motility gastro intestine is portrayed by periods of strong motor activity in empty state-during deprivation conditions. The expected GRT of the unit can be predicted extremely short. However, The GRT must be longer & the MMC is delayed mostly in the consumed state.

Nature of the meal- The flexibility of the stomach could be changed by the feeding of an undigested polymer of fatty acid salts to a fed state of the stomach. The rate at which the

stomach becomes empty and the releases of the drug become prolong only because of these pronouncements.

Caloric content- With the help meal which is high in protein and fats we can upgrade GRT from between 4 to 10 hours.

Frequency of nutriment- The GRT can be enhanced when compared with the one meal caused by the low frequency of MMC.

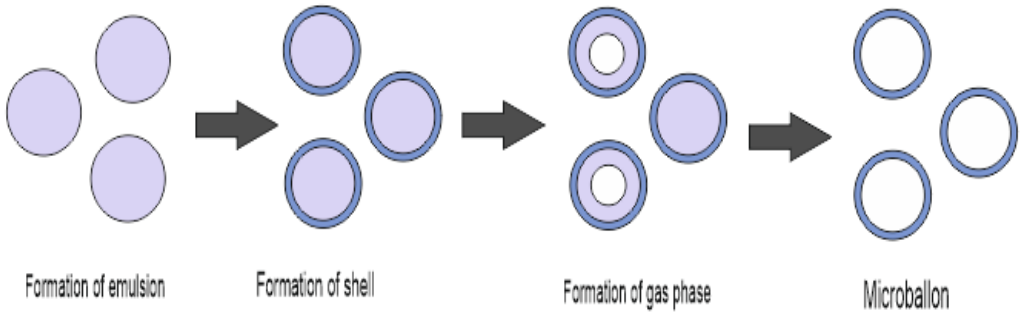
Gender- In general females have more slow purging rate rather than guys.

Mental condition- Stress upgrade the gastric emptying rate while depression makes the slowdown.

Age- Individuals beyond 70 years old have longer GRT.

Disease state- Biological factor of a patient and the state of disease also influence the GRT.[44-54]

Process of formation of microballoons

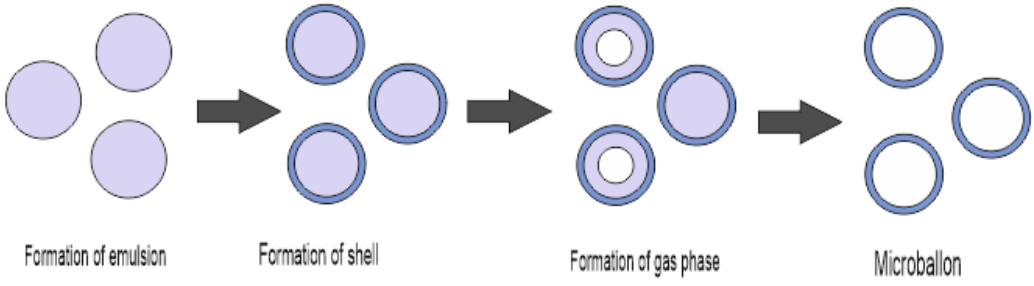


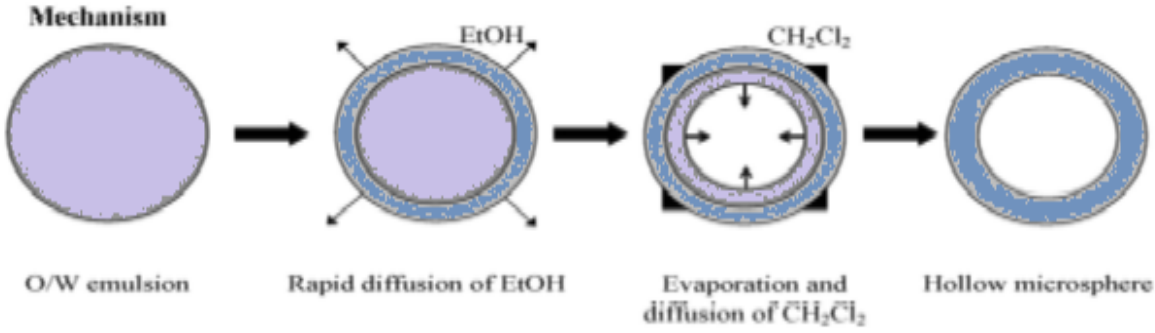
Methods used in the preparation of micro balloon

There are several methods used for preparing the micro balloons. Those depend on the route of administration, duration of drug release, and plasticizer. The different of preparation are

1) Emulsion solvent evaporation method– PVA as an emulsifier is used in this method. initially have the chloroform that contains previously dissolved drugs in it & then this is added to the aqueous phase that contains 0.2 percent solution of PVA. 500 RPM is used to stir the mixture and then by the solvent evaporation method, the rigid microballoon is

solidifying from the droplets. Then wash the microballoons with doubled distilled water, desiccated at room temperature after 24 hours the microballoons were collected



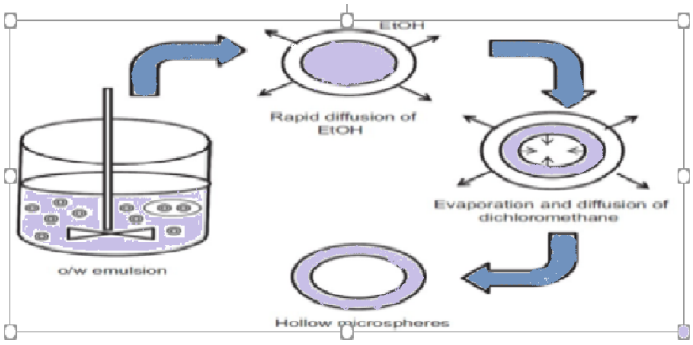


I. Oil in water solvent evaporation- but the polymer should be water-immiscible. some organic solvent such as dichloromethane, methanol, and chloroform Was dissolved within the polymer. The drug is either solvated or diffuse into the polymer mixture with the help of an emulsifying agent, for the formation of an oil-in-water type emulsion, the solution should be emulsified into an aqueous condition. After that, the organic solvent is drawn off with the help of the filtration process the microparticles are separated and collected.

Water-in-oil emulsification solvent evaporation technique - This method of formation of micro balloon is otherwise known as anhydrous emulsification solvent vaporization. To form steady drug-polymer dispersion the Drug and polymers mixture was dissolved in each other at room temperature with vigorous agitation. When in a mixture oil solvent surfactant such as Span is present then the previous mixture is added into the dispersal medium that mostly contains light / heavy liquid paraffin. At this point for complete dissipation of the solvent from the mixture is done by the stirring process with the propeller agitator at a specific period. when the liquid layer is drawn off and segregate fine particles are collected by

seepage through a Whitman filter paper, subsequently, microballons were collected after the washing and drying process and stored in desiccators.

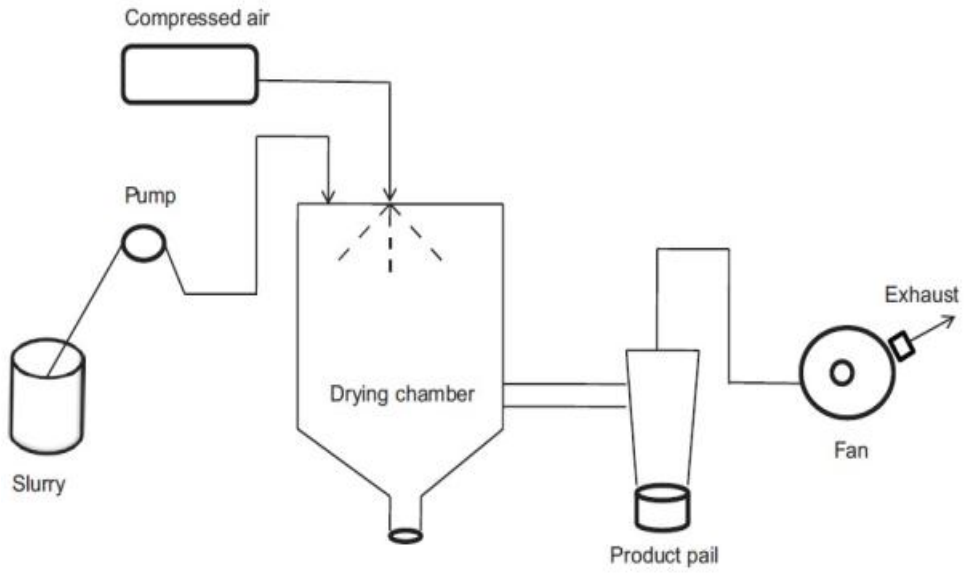
2) Emulsion-solvent diffusion technique- Prepare a combination of ethanol and dichloromethane (1:1) and dissolve the medicament and polymer in it then to the solution of sodium lauryl sulphate the resulting mixture was added dropwise. By using a propeller-type agitator stirring the whole mixture of emulsion at the environmental temperature and 150 rpm for 1 to 4 hours and the established floating micro balloons were dried before washing it with water then store in a desiccator at room temperature.



3) Solvent diffusion-evaporation technique- This technique is the alteration of two techniques solvent evaporation and solvent diffusion method. In this the drug, polymer and 0.1%of surfactants such as PEG were mixed in a solution of ethanol and dichloromethane (1:1) at room temperature, the solution is introduced slowly in 80 ml of 0.46% w/w (may vary) of polyvinyl alcohol as emulsifier & stir the solution using the propeller type agitator for 1 hour for the evaporation of the organic solvent. And at the end filter it.

4) Spray drying method- This is the most liked method by the industry for particle formation and drying. The distribution of particle size, bulk quantity, and shape of all the particles, these properties can be achieved by this method in a single step, it is the best possible process to achieve the aim.[41] organic diluents such as dichloromethane, acetone, etc are used to dissolve the polymer for this method. Then spray the slurry onto the drying oven, the concentration gradient of the solute from small droplets with the richest concentration being at the droplet surface. This happens due to the time of solute diffusion is mostly more than the droplets was evaporated off the solvent by drying. Then toward the formed microsphere, a solid shell appears. Employing cyclone separator, the Detachment of the

solid product from the gases is usually accomplished. the product is collected for later use after the traces of the solvents are evacuated by the vacuum drying.



1. Coacervation phase separation technique- This strategy is relying on the phenomenon that in the organic phase by slow down the solubility of the polymer affects the making of the polymer-rich phase called co-acervates. In the polymer solution, the drug was dispersed. the first polymer makes the separation and merges in the drug particles because an inappropriate polymer was added to the system.[57-64]

5. Factors affecting physicochemical properties of micro balloon

Stirring rate– This is clear-cut that the size of the microsphere is directly affected by the stirring process and its rate so if we increase the speed pf agitation the size of the developed microsphere will be increased. And finally, the conclusion is the speed of agitation over the study range can't break up the bulk of polymer into the fine beads.[65,66]

Temperature– The combination solution of drug and polymer is into an aqueous dispersion of PVA by pouring process at a varying temperature like 23,30,40,50 which results that the preparation increases particle size reduced. Because at high temperature the viscosity of the solution is reduced and the emulsion could break easily.[67]

Plasticizers- Because plasticizers are used, they provide the flexibleness to the surrounding wall of material so under the pressure condition it never gets fragile. It is additionally seen as soon as the increment is happening in plasticizer concentration it was noticed that the delivery of the drug increases.[68]

Solvent ratio- The joining liquids plays a significant role in the micro balloon formation. While bridging liquids are used in less amount, they give irregular shape microsphere yet when used in a large amount. Bridging liquids prevents the emulsion from solidifying. The proportion of the solvent system affects the morphology of the microsphere. In this way, to have the best shape microsphere the ratio of ethanol & dichloromethane 2:1 gives the best outcome with a spherical shape.[69]

Viscosity- At the low concentration of the polymer micro balloon with small shape can be formed and they provide the faster release of the drug because it has a wide effective surface to expose the dissolution medium.[70]

Effect of the solvent- Different solvent shows a distinctive effect on the microsphere when dichloromethane is used as a solvent system. It was noticed by the observation that the prepared microspheres are not all spherical. For the solution of this problem, methanol & dichloromethane both are beneficial in combination. The microsphere obtained with this combination are spherical by the surface isn't smooth. On the behalf of their boiling point, various solvents are screened just to avoid this problem like DCM,[39] acetone,[56] methanol[64] & ethanol.[78] Because this is observed that B.P increases from DCM to ethanol, so most of the time ethanol is used. So, most of the drug those are soluble in water and water-insoluble polymer showed dissolve in ethanol. As we all know that ethanol has high B.P in comparison with another solvent such as DCM, acetone, methanol, which prevent sudden polymer precipitation. Which results in a spherical shape and smoother surface.[71]

Emulsifier concentration- The concentration of emulsifier also affects the particle size. It was noticed that when the concentration of emulsifier decreases the particle diameter and size distribution increases the work of emulsifier Is to decreases the interfacial tension between the dispersed beads from collision and coalescence.[72-74]

Evaluation of floating micro balloon

Particle size

With the help of a light microscope, the size of particle for the micro balloons was estimated, and the mean micro balloons size was determined by average estimating 100 particles by using a previously set usual micrometre.

Bulk density

Bulk density is the ratio of powder weight and its volume. Take a 25 ml measuring cylinder then 10 grams of sample's granules put In it. Then without disturbing the cylinder note, the volume that is occupied by the cylinder and by using this equation calculates the bulk density. (values expressed in gm/cm3)

$$\text{Bulk density} = \frac{\text{Weight of sample (s)}}{\text{Volume of a sample (v)}}$$

Tapped density

This can be estimated by accurately measuring the sample powder of 10 gm and placed in a measuring cylinder with a capacity of 25 ml. at the interval of 2 seconds knocked it 100 times onto a tough-wooden top, during a specific time interval. by recording the final volume, we can estimate the tapped density with the help of the following condition. (values expressed in gm/cm3)

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

Carr's index (%)

Most of the time the flowability of a powder can be estimated by The Carr‟s index. As per this Carr index below 15% has good flowability and more than 25% is considered to be a sign of poor flowability. blending flow property depends upon the Compressibility index. the compressibility of a powder can be defined in terms of The Carr‟s index. It is calculated by the formula. (Values as given in)

$$\text{Carr's index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Carr's index indicates the powder flow

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

repose angle (θ)

repose angle or we can say that angle of repose is flowability represented by the angle of repose. Firstly, balance the funnel in such a way that the funnels' stem lies above the level of the surface to let the powder flow from the funnel so that the tip of the funnel touches the pile's height. draw a boundary line along with the circumference the diameter of the pile can be regulated by measuring the average of three breadths. Then compute the angle of repose by the following formula.

$\tan \theta = \frac{h}{r}$

$\theta = \tan\text{-}1 \left(\frac{h}{r}\right)$

Where θ belongs to the angle of repose,

h belongs to the height of the pile;

r belongs to the radius of the pile

Relationship between angle of repose (θ) and flowability

Repose angle(θ)	Flowability
>40	Very poor
30-40	passable
25-30	Good
<25	Excellent

Hausner's ratio

The Hausner‟s proportion is the representative of the ability of a powder to compress. We can calculate it by this Equation,

Hausner′s ratio = Tapped density × 100

Bulk density-

The Hausner‟s proportion can be frequently used to represent the quality of a powder to flow. More than the value of 1. assumed as poor flowability. The observations for the flow properties determinations were brought down.

Flow character	Hausner's ratio
very poor	1.46-1.59
poor	1.35-1.45
passable	1.26-1.34
fair	1.19-1.25
good	1.11-1.18
excellent	1-1.11

Percentage yield

The fraction of the actual weight of a product and the total volume of all non-volatile components those are utilized by floating micro balloons for their preparation the percentage yield of floating micro balloons could be deliberated and can be resented in term of the following equation

$$\% \text{ yield} = = \frac{\text{real weight of product}}{\text{total weight of drug and Excipient}} \times 100$$

Drug entrapment efficiency (DEE)

To measure the Drug entrapment efficiency, crush the average amount of microballoon and extract it within aliquots of 0.1N HCl repeatedly then transfer the distillate to a volumetric flask with the capacity of 100 ml and make up the volume to the final level with HCL. Filter out the solution and check the absorbance against an appropriate blank with the help of a spectrophotometer. Then evaluate how much amount of drug entrapped by the microballoon with the given formula.

$$\text{DEE} = \frac{\text{drug present actually}}{\text{theoretical drug}} \text{ x } 100$$

In vitro buoyancy

USP dissolution test apparatus II is utilized to study the Floating behavior of hollow micro balloons by spreading the micro balloons (average 50 mg) in the solution of 0.1 N HCl that contains 0.02% of Tween 80 work as a surfactant (900 ml). Then agitate the whole medium at 100 RPM with the help of a paddle by maintaining the temperature at 37°C. after that process, the floating and settled portion separately collected. Then microballoon were collected after the filter and drying process. With the help of this equation, the percentage buoyancy was determined.

$$\% \text{ buoyancy of micro balloons} = \frac{weight\ of\ floating\ microballoon}{the\ initial\ weight\ of\ floating\ microballoon} \text{ x } 100$$

Invitro-drug release of micro balloons

USP paddle-type dissolution assembly is used to evaluate the in-vitro delivery of the medicament. measure approx 900 ml of the dissolution medium because it is equal to the gastric volume, accurately weigh microballoon those are equal to the dose were added and agitated at 100 rpm at 37 ± 0.5 ºC. then pulled out some samples within some specific time interval and analysed. A suitable analytical method is used to analyse the data.

Morphological study using SEM

To study the internal or external morphology of a microballoon ordinarily scanning electron microscopy (SEM) apparatus is used.

Stability studies

The samples were further kept in a stability chamber after sealing in an aluminium package and coat with polyethylene. The temperature was maintained between 40-45°C and 75% RH for a specific period of time mostly (3 months). After this time period, the samples were taken off and reviewed for the physical appearance and drug content.[75-88]

Applications of floating microballoons

- Because microballon has constrained absorption in the upper GIT so drugs that have poor bioavailability, Floating micro balloons proves a very effective approach in the delivery. the absorption of these systems can be maximized and the availability of several drugs enhanced e.g. Furosemide, Riboflavin, etc.
- The floating micro balloons are also utilized as bearers for some drugs with purported absorption windows, substances like that, for instance, anti-viral, anti-fungal, and anti-microbial operators are taken up in a manner of from unmistakable site of the GI mucosa.
- Gastro retentive microballoons reduced major adverse effects in such an extremely viable method that irritate the gastric environment, for example, floating micro balloons of nonsteroidal calming drugs.
- Floating micro balloons are particularly compelling in the conveyance of slightly soluble and insoluble drugs. It is referred to that as the dispersible of drugs diminishes, the time accessible for sedate resolution turns out to be less sufficient and hence the travel time turns into a huge factor influencing drug retention. For feebly essential medications that are inadequately dissolvable at a basic pH, hollow micro balloons may keep away from a chance for solvency to turn into the rate-limiting step in discharge by confining such medications to the GIT, for instance, Verapamil hydrochloride. The gastro-retentive floating micro balloons will change advantageously the assimilation profile of the dynamic operator, subsequently improving its bioavailability
- Some particular drugs those absorbed by the stomach specifically or on the other hand, the proximal piece of the duodenum, ileum, jejunum such frameworks are especially points of interest. drug waste could be diminished by focusing on a moderate conveyance of drug to the stomach.

- These micro balloons have a major application in that they release drugs over a drawn-out period and eliminate the medicament in a sustained manner.
- Site-specific absorbing drugs should be in the upper part of the gastrointestinal tract and have poor bioavailability. Such kind of drugs is potential candidates those can be formulated as floating drug delivery systems thereby boosting their absorption.
- These frameworks are especially profitable for drugs that are explicitly absorbed from the stomach or the proximal piece of the small intestine.[89-99]

List of drugs formulated as microballoons

S. no	Drugs	Polymers	Method	Ref.
1.	Atenolol	Ethyl cellulose & HPMC	Emulsion solvent evaporation technique	[100]
2.	Curcumin	Ethyl cellulose, Eudragit S100 & HPMC	Emulsion solvent evaporation technique	[101]
3.	Tolperisone	Ethyl cellulose (EC), & HPMC 15 cPs	Non-aqueous solvent evaporation technique	[102]
4.	Famotidine	HPMC and Ethyl cellulose (EC)	Solvent evaporation (Oil-in-water emulsion) technique	[103]
5.	Captopril	HPMC(K4M) and Ethyl cellulose (EC)	Ionotropic gelation technique	[104]
6.	Ketoprofen	Eudragit S100 and Eudragit L 100	Emulsion solvent diffusion method	[105]
7.	Ketorolac trometamol.	Ethyl cellulose, HPMC K4M, Eudragit R100 &Eudragit S100	Emulsion solvent diffusion method	[106]
8.	Glipizide	Acrycoat S100, Eudragit RS100.	Emulsion solvent diffusion technique	[107]
9.	Rabeprazole	HPMC K15M and Ethyl cellulose	Emulsion solvent Evaporation	[108]
10.	Orlistat	Eudragit S	Emulsion solvent Evaporation	[109]
11.	Esomeprazole	HPMC and Methyl cellulose	Solvent evaporation method	[110]
12.	Cimetidine	HPMC and Ethylcellulose	Solvent evaporation method	[111]
13.	Stavudine	Eudragit RS100	Emulsion solvent diffusion	[112]
14.	Metformi	Eudragit RS100 and Eudragit RL	Non aqueous solvent evaporation	[113]
15.	Aceclofenac	Ethyl cellulose	Solvent evaporation	[114]

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