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FLOATING MICROSPHERES - AN EXCELLENT APPROACH FOR GASTRIC RETENTION

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ABSTRACT

Floating microspheres are multiple unit drug delivery systems which are designed to obtain prolonged or controlled drug delivery to enhance bioavailability, stability and to target the drug to a specific site at a predetermined rate. A controlled drug delivery system with the prolonged residence time in the stomach can be of great practical importance for drugs with an absorption window in the upper small intestine. The main limitations are attributed to the inter and intra-subject variability of gastrointestinal (GI) transit time and to the non-uniformity of drug absorption throughout the alimentary canal. Floating or hydrodynamically controlled drug delivery systems are used in such applications. Gastro retentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Floating microspheres have been gaining attention due to the uniform distribution of these multiple-unit dosage forms in the stomach, which results in more reproducible drug absorption and reduced risk of local irritation. Such systems have more advantages over the single unit dosage forms. The present review briefly addresses the physiology of the gastric emptying process with respect to floating drug delivery systems. The purpose of this review is to bring together the recent literature with respect to the method of preparation, and various parameters affecting the performance and characterization of floating microspheres.

Keywords: Floating microspheres, Gastro Retention, Short half-life, Solvent diffusion.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site of the body, to achieve promptly and then maintain the desired therapeutic drug concentration that elicits the pharmacological action and to minimize the incidence and the severity of unwanted adverse effects. To achieve this goal, it would be advantageous and more convenient to maintain a dosing frequency to once, or at most, a twice-daily regimen [1].

Drugs that are easily absorbed from the GIT and have a short biological half-life and eliminated quickly from the blood circulation require frequent dosing. To avoid this problem, the oral controlled release (CR) formulations have been developed in an attempt to release the drug slowly into the GIT and maintain a constant drug concentration in the serum for longer period of time [2].To increase the gastric emptying time and control over the release of the drug from the devices, the increasing sophistication of

delivery technology will ensure the development of increasing number of gastro retentive drug delivery systems to optimize the delivery of molecules that exhibit low bioavailability and extensive first pass metabolism. A gastric floating drug delivery system can overcome at least some of these problems and is particularly useful for drugs that are primarily absorbed in the duodenum and upper jejunum segments, and it can prolong retention times of dosage forms in the GIT, and thereby improve their oral bioavailability [3]. Floating microspheres are gastro-retentive drug delivery systems based on non-effervescent approach. Hollow microspheres are in strict sense, spherical empty particles without core. These microspheres are characteristically free flowing powders having a size less than 199 μm and remain buoyant over gastric contents and for prolonged period. Gastro-retentive floating microspheres are low-density systems that have sufficient buoyancy to float over gastric contents and remain in stomach for prolonged period. As the system floats over gastric contents, the drug is released slowly at desired rate resulting in increased gastric retention with reduced fluctuations in plasma drug concentration [4]. The gastric emptying time (GET) and the variation in the pH in the different segments of gastrointestinal tract (GIT) are the major challenges in the development of oral controlled release drug delivery systems. Gastroretentive system can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drug in the GIT [5]. The prolongation of gastric residence time (GRT) of delivery system could be achieved by the mechanism of mucoadhesion, simultaneous administration of pharmacological agents that delay the gastric emptying [6]. One of the methods for enhancement of GRT is based on the mechanism of floatation. Wherein the delivery systems are less dense than the gastric fluid. Floating single dosage form, also called hydro dynamically balanced systems (HBS), have been extensively studied. Floating systems, first described by Davis in 1968, are low-density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period [7]. The system floats over the gastric contents, releasing the drug slowly at the desired rate, which not only results in increased GRT but also reduces fluctuation in plasma drug concentration[8].

CLASSIFICATION OF FDDS BASED ON MECHANISM OF BUOYANCY

1) Single unit floating dosage systems

Single unit dosage forms are easiest to develop but suffers from the risk of losing their effects too early due to their all- or- none emptying from the stomach and, thus they may cause high variability in bioavailability and local irritation due to large amount of drug delivered at a particular site of the gastro intestinal tract [9].

A) Noneffervescent systems

One or more gel forming, highly swellable, cellulosic hydrocolloids (e.g. hydroxyl ethyl cellulose, hydroxyl propyl cellulose, hydroxypropyl methyl cellulose [HPMC] and sodium carboxy methyl cellulose), polysaccharides, or matrix forming polymers(e.g., polycarbophil, polyacrylates, and polystyrene) are incorporated in high level (20- 75% w/w) to tablets or capsules [10,11]. For the preparation of these types of systems, the drug and the gelforming hydrocolloid are mixed thoroughly. After oral administration this dosage form swells in contact with gastric fluids and attains a bulk density of < 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel- like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass.

B) Effervescent systems or gas generating systems

These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, e.g. sodium bicarbonate, tartaric acid, and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, CO2 is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms. The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1.

2) Multiple units floating dosage systems

Single unit formulations are associated with problems such as sticking together or being obstructed in gastrointestinal tract, which may have a potential danger of producing irritation. Multiple unit systems avoid the 'all- or- none' gastric emptying nature of single unit systems. It reduces the intersubject variability in absorption and the probability for dose dumping is lowers [12].

A) Noneffervescent systems

A little or no much report was found in the literature on noneffervescent multiple unit systems, as compared to the effervescent systems. However, few workers have reported the possibility of developing such system containing indomethacin, using chitosan as the polymeric excipient. A multiple unit HBS containing indomethacin as a model drug prepared by extrusion process is reported. A mixture of drug, chitosan and acetic acid is extruded through a needle, and the extrudate is cut and dried. Chitosan hydrates float in the acidic media, and the required drug release could be obtained by modifying the drug- polymer ratio.

B) Effervescent systems

A multiple unit system comprises of calcium alginate core and calcium alginate/PVA membrane, both separated by an air compartment was prepared. In presence of water, the PVA leaches out and increases the membrane permeability, maintaining the integrity of the air compartment. Increase in molecular weight and concentration of PVA, resulted in enhancement of the floating properties of the system. Freeze- drying technique is also reported for the preparation of floating calcium alginate beads. Sodium alginate solution is added drop wise into the aqueous solution of calcium chloride, causing the instant gelation of the droplet surface, due to the formation of calcium alginate. The obtained beads are freeze-dried resulting in a porous structure, which aid in floating. The authors studied the behaviour of radiolabeled floating beads and compared with nonfloating beads in human volunteers using gamma scintigraphy. Prolonged gastric residence time of more than 5.5 hour was observed for floating beads. The nonfloating beads had a shorter residence time with a mean onset emptying time of 1 hr [13].

C) Floating microspheres

A controlled release system designed to increase its residence time in the stomach without contact with the mucosa was achieved through the preparation of floating microspheres. Techniques involved in their preparation include simple solvent evaporation, and solvent diffusion and evaporation. The drug release and better floating properties mainly depend on the type of polymer, plasticizer and the solvents employed for the preparation. Polymers, such as polycarbonate, Eudragit® S and cellulose acetate, are used in the preparation of hollow microspheres, and the drug release can be modified by optimizing the amount of polymer and the polymerplasticizer ratio [14].

3) Raft forming systems

The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. The raft floats because of the buoyancy created by the formation of CO2 and act as a barrier to prevent the reflux of gastric Contents like HCl and enzymes into the esophagus. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluids [15].

MECHANISM OF FLOATING MICROSPHERE

Floating systems or Hydro dynamically controlled drug delivery systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain in stomach for prolonged period.

While the dosage form floats on the gastric contents, the drug is released continuously at the desired rate from the system resulting in increased gastric retention with reduced fluctuations in plasma drug concentration. When floating microspheres come in contact with gastric fluid all other ingredients hydrate to form a colloidal gel barrier that controls the rate of fluid penetration into the device and consequent drug release. As the outer surface of the microspheres dissolves, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air entrapped by the polymer lowers

the density and confers buoyancy to the microspheres but a minimal gastric content needed to allow proper achievement of buoyancy [16-18].

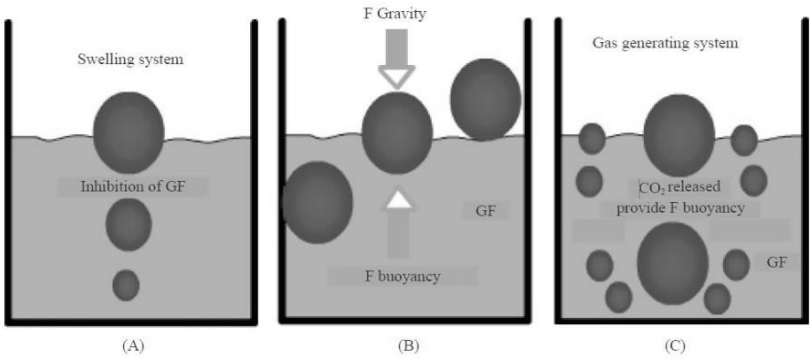

Fig 1 Mechanism of floating systems

POLYMERS USED IN MICROSPHERE

Microspheres used usually are polymers. They are classified into two types:

1) Synthetic Polymers

2) Natural polymers

1. Synthetic polymers are divided into two types.

(A) Non-biodegradable polymers: Poly methyl methacrylate acrolein (PMMA), Glycidyl methacrylate, Epoxy polymers.

(B) Biodegradable polymers: Lactides and Glycolides and their copolymers, Poly alkyl cyano acrylates, Polyanhydrides and Poly-ε-caprolactone (PCL).

2. Natural polymers obtained from different sources like proteins, carbohydrates and chemically modified carbohydrates.

(A) Proteins: Albumin, Gelatin and Collagen.

(B)Carbohydrates: Agarose, Carrageenan, Chitosan, Starch [19].

(C) Chemically modified carbohydrates: Poly dextran, Poly starch.

THE ADVANTAGES OF FLOATING MICROSPHERES

1. Improves patient compliance by decreasing dosing frequency.
2. Bioavailability enhances despite first pass effect because fluctuations in plasma drug concentration is avoided, a desirable plasma drug concentration is maintained by continuous drug release.
3. Gastric retention time is increased because of buoyancy.
4. Drug releases in controlled manner for prolonged period.
5. Site-specific drug delivery to stomach can be achieved.
6. Enhanced absorption of drugs which solubilise only in stomach.
7. Superior to single unit floating dosage forms as such microspheres releases drug uniformly and there is no risk of dose dumping.
8. Avoidance of gastric irritation, because of sustained release effect, floatability and uniform release of drug through multiparticulate system [20].

DISADVANTAGES

1. They are not suitable candidates for drugs with stability or solubility problem in stomach.
2. FDDS require sufficiently high level of fluid in stomach so that the system can float and thus sufficient amount of water (200-250 ml) of water to be taken together with FDDS.
3. Drugs having irritant effect on gastric mucosa are not suitable candidates for FDDS.
4. Drugs which are absorbed along the entire GIT and which undergo first pass metabolism may not be desirable e.g. nifedipine.

DRUGS SUITABLE FOR DESIGNING GASTRO-RETENTIVE DOSAGE FORM

1. Drugs those are locally active in the stomach e.g., misoprostol and antacid.
2. Drugs that have narrow absorption window in the gastro intestinal tract. e.g., riboflavin and levodopa.
3. Drugs absorbed primarily from the stomach and upper part of the stomach e.g., Calcium supplements and chlordiazepoxide.
4. Drugs that degrade in the colon e.g., ranitidine HCl and metronidazole

5. Drugs that disturb the normal colonic bacteria. E.g., amoxicillin trihydrate.
6. Drugs that exhibit low solubility at high pH values e.g., diazepam, chlordiazepoxide, and verapamil HCl [21].

METHODS OF PREPARATION OF MICROSPHERES

1. Emulsion solvent evaporation technique

Drug is dissolved in polymer which was previously dissolved in volatile organic solvent and the resulting solution is added to aqueous phase containing emulsifying agent. The above mixture was agitated at 500 rpm then the drug and polymer was transformed into fine droplet which solidified into rigid microspheres by solvent evaporation and then collected by filtration and washed with demineralised water and desiccated at room temperature for 24 hrs.

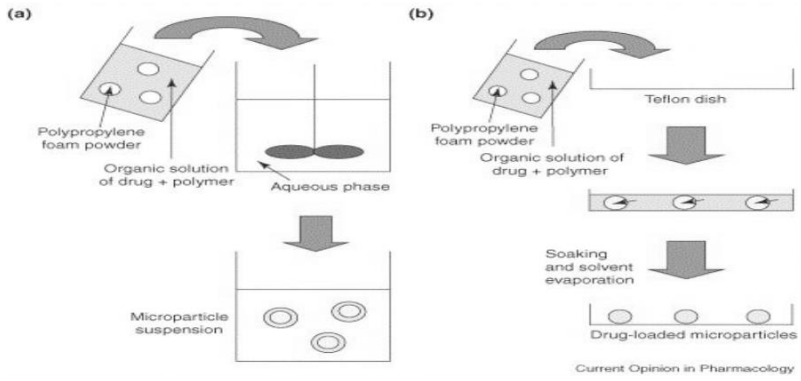

Fig 2 Emulsion Solvent Evaporation Technique

2. Emulsion cross linking method

In this method drug was dissolved in aqueous gelatin solution which was previously heated for 1 hr at 400C. The solution was added drop wise to liquid paraffin while stirring the mixture at 1500 rpm for 10 min at 350 C, results in w/o emulsion then further stirring is done for 10 min at 150C. Thus the produced microspheres were washed respectively three times with isopropyl alcohol which then air dried and dispersed in 5mL of aqueous glutaraldehyde saturated toluene solution at room temperature for 3 hours for cross linking and then was treated with 100mL of 10mmglycine solution containing 0.1 %w/v of tween 80 at 37 0C for 10 min to block unreacted glutaraldehyde. Examples of this technique are Gelatin microspheres.

3. Double emulsion technique

This method can be used with both the natural as well as synthetic polymers. The aqueous protein solution is dispersed in a lipophilic organic continuous phase. This protein solution may contain the active constituents. The continuous phase is generally consisted of the polymer solution that eventually encapsulates of the protein contained in dispersed aqueous phase. The primary emulsion is subjected then to the homogenization before addition to the aqueous solution of the poly vinyl alcohol (PVA). This results in the formation of a double emulsion. The emulsion is then subjected to solvent removal either by solvent evaporation or by solvent extraction. Then collect microspheres by filtration and washed with demineralized water.

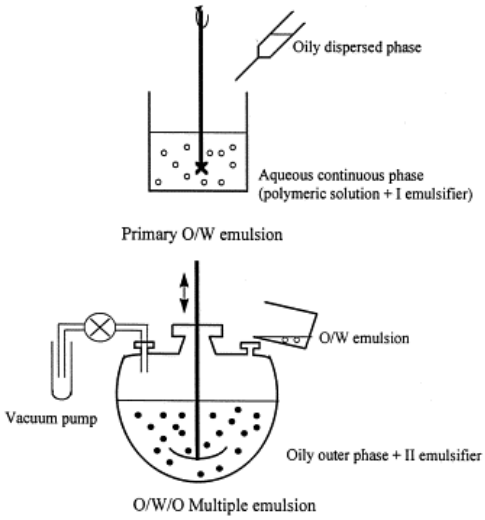

Fig 3 Double emulsion technique

4. Co-acervation method

In this method, the drug particles are dispersed in a solution of the polymer and an incompatible polymer is added to the system which makes first polymer to phase separate and engulf the drug particles. Addition of non-solvent results in the solidification of polymer.

5. Spray drying technique

The two processes are named spray drying and spray congealing. The polymer is first dissolved in a suitable volatile organic solvent. The drug in the solid form is then dispersed in the polymer solution under +high-speed homogenization. This dispersion is then atomized in a stream of hot air. The atomization leads to the formation of the small droplets or the fine mist from which the solvent evaporates instantaneously leading the formation of the microspheres in a size range 1 -100 μm.

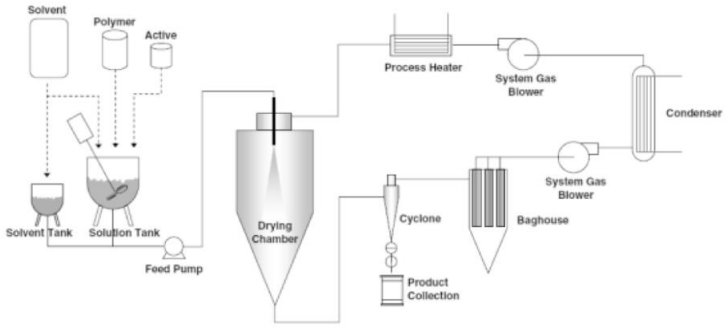

Fig 4 Spray drying technique

6. Hydroxyl appetite (HAP) microspheres in sphere morphology

This was used to prepare microspheres with peculiar spheres at first o/w emulsion was prepared by dispersing the organic phase (Diclofenac sodium containing 5% w/w of EVA and appropriate amount of HAP) in aqueous phase of surfactant. The organic phase was dispersed in the form of tiny droplets which were surrounded by surfactant molecules this prevented the droplets from co-solvencing and helped them to stay individual droplets. While stirring the DCM was slowly evaporated and the droplets solidify individual to become microspheres.

7. Chemical methods

This method uses monomers/prepolymers as starting materials. These methods involve chemical reactions along with microsphere formation. These include suspension polymerization, emulsion polymerization, dispersion and interfacial methods. Among them emulsion polymerization method is widely used in drug delivery.

8. Polymerization techniques

The polymerization techniques conventionally used for the preparation of the microspheres are mainly classified as

a. Normal polymerization

b. Interfacial polymerization

(Both are carried out in liquid phase)

a. Normal polymerization

It is carried out using different techniques as bulk, suspension, precipitation, emulsion and micellar polymerization processes. In bulk, a monomer or a mixture of monomers along with the initiator or catalyst is usually heated to initiate polymerization. Polymer so obtained may be moulded as microspheres. Drug loading may be done during the process of polymerization. Suspension polymerization also referred as bead or pearl polymerization. Here it is carried out by heating the

monomer or mixture of monomers as droplets dispersion in a continuous aqueous phase. The droplets may also contain an initiator and other additives. Emulsion polymerization differs from suspension polymerization as due to the presence initiator in the aqueous phase, which later on diffuses to the surface of micelles. Bulk polymerization has an advantage of formation of pure polymers.

b. Interfacial polymerization

Involves reaction of various monomers at the interface between the 2 immiscible liquid phases to form a film of polymer that essentially envelopes the dispersed phase. In this 2 reacting monomers are employed one of which is dissolved in the continuous phase while the other being dispersed in the continuous phase. Monomer present in either phases diffuse rapidly 7 polymerize rapidly at the interface. If the polymer is soluble in the droplet it will lead to the formation of monolithic type of the carrier on the other hand if polymer is insoluble in the monomer droplet, the formed carrier is of capsular (reservoir) type. The degree of polymerization can be controlled by the reactivity of monomer chosen, their concentration, and composition of the vehicle of either phases and by the temperature of the system. The particle size can be controlled by controlling the droplets or globule size of the disperse phase. The polymerization reaction can be controlled by maintaining the concentration of the monomers, which can be achieved by the addition of an excess of the continuous phase.

9. Hot melt microencapsulation

The polymer is first melted and then mixed acid solid drug particle or liquid drugs. This mixture is suspended in an immiscible solvent and heated to 50C above the melting point of the polymer under continuous stirring. The emulsion is then cooled below the melting point until the droplets solidify [22-26].

EVALUATION OF FLOATING MICROPARTICULATE DRUG DELIVERY

Particle size

The particle size of the microspheres is measured using an optical microscopy and mean size is calculated by measuring 200-300 particles with the help of a calibrated ocular micrometer [27].

Bulk density

Bulk density is defined as the mass of powder divided by bulk volume. Accurately weighed 10 gm sample of microsphere is placed into 25 ml measuring cylinder. Volume occupied by the microsphere is noted without disturbing the cylinder and the bulk density was calculated using the equation (expressed in gm/cm3) [28].

$$\text{Bulk Density} = \frac{\text{Weight of microspheres}}{\text{Bulk Volume}}$$

Tapped density

Tapping method is used for the determination of tapped density. In this method, 10 gm of hollow microsphere sample is placed in 25 ml measuring cylinder and dropped at a height of one inch onto a hard wooden surface 100 times at an interval of 2 seconds. The final volume was recorded and the tapped density is calculated by the following equation (expressed in gm/cm3) [28].

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

Hausner ratio

The Hausner ratio indicates the compressibility and flow property of a powder [29]. This is calculated from the values of bulk density and tapped density by using the formula:

Hausner ratio = [Tapped density / Bulk density]

A Hausner ratio greater than 1.25 is an indication of poor flowability.

Carr's index

The Carr's index indicates of the flowability and compressibility of a powder [29]. This is calculated from the values of bulk density and tapped density by using the formula:

Carr's Index (%) = Tapped density-Bulk density/ Tapped density x 100

Angle of repose

The angle of repose is indicative of flowability of the substance. This can be determined by funnel method. The height of the funnel is adjusted in such a way that stem is 2.5 cm above the horizontal surface. The sample powder was allowed to flow from the funnel adjusted at a height of 2.5 cm from the stem. The diameter of the pile was determined by drawing a boundary along the circumference of the pile and taking the average of three diameters. It is calculated by the formula Angle of repose (θ) = tan-1 (h/r) Where, θ is angle of repose, 'h' is height of the pile; r is the radius of the pile [29,30].

Percentage yield

Percentage yield of floating microspheres was calculated by dividing actual weight of product to total amount of all non-volatile components that are used in the preparation of floating microspheres and is represented by following formula [31]:

% yield = actual weight of product/ total weight of drug and excipients x 100

Morphological Study using SEM

The external and internal morphology of the microspheres is studied by using scanning electron microscopy (SEM) [31].

FT-IR (Fourier Transform Infra Red)

The drug polymer interaction and also degradation of drug while processing for microencapsulation can be determined by FTIR [32].

Drug entrapment efficiency (DEE)

The amount of drug entrapped is estimated by crushing the microspheres and extracting with suitable solvent repeatedly. The extract is filtered and the absorbance is measured by spectrophotometer. The amount of drug entrapped in the microspheres is calculated by the following formula [33]:

DEE = Total drug - free drug/ Total drug x 100

***In vitro* buoyancy**

Floating microspheres should be placed in 100 ml of the simulated gastric fluid (SGF, pH 2.0) containing 0.02% w/v Tween 20. The mixture is stirred at 100 rpm with a magnetic stirrer. After 8 h, the layer of buoyant microspheres is pipetted and separated by filtration. Particles in the sinking particulate layer are separated by filtration. Particles of both types are dried in desiccators until constant weight is achieved. Both the fractions of microspheres are weighed and buoyancy is determined by the weight ratio of floating particles to the sum of floating and sinking particles [34].

% buoyancy of microspheres = weight of floating microshperes / initial weight of floating Microspheres x 100

Dissolution test (*in vitro* drug release) of microspheres

In vitro dissolution studies can be carried out in a USP paddle type dissolution assembly. Drug dose equivalent microspheres are added to 900 ml of the dissolution medium and stirred at 100 rpm at 37 ± 0.5 ºC. Samples are withdrawn at a specified time interval and analyzed by any suitable analytical method, such as UV spectroscopy [35].

Thermal analysis

Thermal analysis of microspheres and its component can be done by using (DSC), Thermo Gravimetric Analysis (TGA) and Differential Thermometric Analysis (DTA). Accurately the sample was weighed and heated on alumina pan at constant rate of 10oC/min under nitrogen flow of 40 ml/min [36].

Floating studies

This test is to determine the floating time of the system, performed in simulated gastric fluid or 0.1 M HCl maintained at 37°C, by using USP dissolution apparatus. The time taken by the dosage form to float is termed as floating lag time and time for which the dosage form floats is termed as floating time [37].

Swelling studies

Swelling studies were performed to calculate molecular parameter of the swollen polymers. Swelling studies was determined by using, dissolution apparatus, optical microscopy, H1NMR imaging, Confocal Laser Scanning, and Light Scattering Imaging [37].

Stability studies

Optimized formulation was sealed in aluminium packaging, coated inside with polyethylene. The samples were kept in the stability chamber maintained at 40 ± 2ºC and 75% ± 5 % RH for 3 months. At the end of studies, samples were analyzed for the physical appearance and drug content [38].

APPLICATIONS

1. Gastro retentive floating microspheres are very effective in the reduction of major adverse effect of gastric irritation; such as floating microspheres of non-steroidal anti-inflammatory drugs i.e. indomethacin are beneficial for rheumatic patients.
2. Floating microspheres are very effective approach in delivery of drugs that have poor bioavailability because of their limited absorption in the upper GIT. These systems efficiently maximize their absorption and improve the bioavailability of several drugs. e.g furosemide, riboflavin etc.
3. The higher dose of drugs can be reduced due to increase in gastric retention time which led to low dose frequency.
4. Drugs that have poor bioavailability because of site specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption.
5. These systems can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral controlled release formulation, hence, can be overcome with these systems. These systems have bulk density of <1, as a result of which they can float on the gastric contents.
6. These systems are particularly advantages for drugs that are specifically absorbed from stomach or the proximal part of the small intestine e.g. riboflavin furosemide and misoprostal. By targeting slow delivery of misoprostol to the stomach, desired therapeutic level could be achieved and drug waste could be reduced.

7. These systems provide an easy way of maintaining constant blood level with an ease of administration and better patient compliance.
8. Hollow microspheres can greatly improve the pharmacotherapy of the stomach through local drug release, leading to high drug concentrations at the gastric mucosa, thus eradicating *Helicobacter pylori* from the sub-mucosal tissue of the stomach and making it possible to treat stomach and duodenal ulcers, gastritis and oesophagitis.
9. The drugs recently reported to be entrapped in hollow microspheres include Prednisolone, Lansoprazole, Celecoxib, Piroxicam, Theophylline, Diltiazem hydrochloride, Verapamil hydrochloride and Riboflavin, Aspirin, Griseofulvin, Ibuprofen, Terfenadine.
10. Floating microspheres can greatly improve the pharmacotherapy of stomach through local drug release. Thus, eradicating *Helicobacter pylori* from sub-mucosal tissue of the stomach are useful in the treatment of peptic ulcers, chronic gastritis, gastro esophageal reflux diseases etc. Floating bio adhesive microspheres of aceto hydroxamic acid are formulated for treatment of *Helicobacter pylori* infection. Hollow microspheres of ranitidine HCl are also developed for the treatment of gastric ulcer.
11. These microspheres systems provide sustained drug release behavior and release the drug over a prolonged period of time. Hollow microspheres of tranilast are fabricated as a floating controlled drug delivery system [39].

CONCLUSION

Floating microspheres has emerged as an efficient approach for enhancing the bioavailability and controlled delivery of various therapeutic agents. Significant attempts have been made worldwide to explore these systems according to patient requirements, both in terms of therapeutic efficacy and compliance. Floating microspheres as gastro retentive dosage forms precisely control the release rate of target drug to a specific site and facilitate an enormous impact on health care. Optimized multiunit floating microspheres are expected to provide clinicians with a new choice of an economical, safe and more bioavailable formulation in the effective management of diverse diseases. These systems also provide tremendous opportunities in the designing of new controlled and delayed release oral formulations, thus extending the frontier of futuristic pharmaceutical development. Increased sophistication of this system will ensure the successful advancements in the avenue of gastro retentive microspheres therapy so as to optimize the delivery of molecules in a more efficient manner.

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