IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
March 2023 Vol.:26, Issue:4

A Review: Gastro Retentive Dosage Form with Special Emphasis on Floating Beads

IJPPR
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An official Publication of Human Journals
ISSN 2349-7203
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Submitted: 22 February 2023
Accepted: 28 February 2023
Published: 30 March 2023

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: Floating dosage form, floating beads, method of preparation, and evaluation of beads.

ABSTRACT

Any drug delivery system's primary goal is to achieve the desired drug concentration in blood or tissue, which is therapeutically efficacious and nontoxic over an extended length of time. Floating beads have a gastro retentive function without changing gastric emptying rate and are utilized for controlled medication release. Drugs with a limited window of absorption in a specific area of the gastrointestinal tract can help increase absorption and bioavailability by using floating drug delivery systems that can be kept in the stomach this can accomplish by utilizing different polymers. They exhibit significant patient benefits. One innovative medication delivery technique to increase stomach retention duration is floating beads. Several gastro-retentive drug delivery methods, including floating and nonfloating.

INTRODUCTION

Due to its simplicity of administration, patient compliance and adaptability in formulation, oral medication delivery is by far the preferred method of drug delivery. Oral dosage formulations have advanced significantly, going from instant release to site-specific delivery.[1]

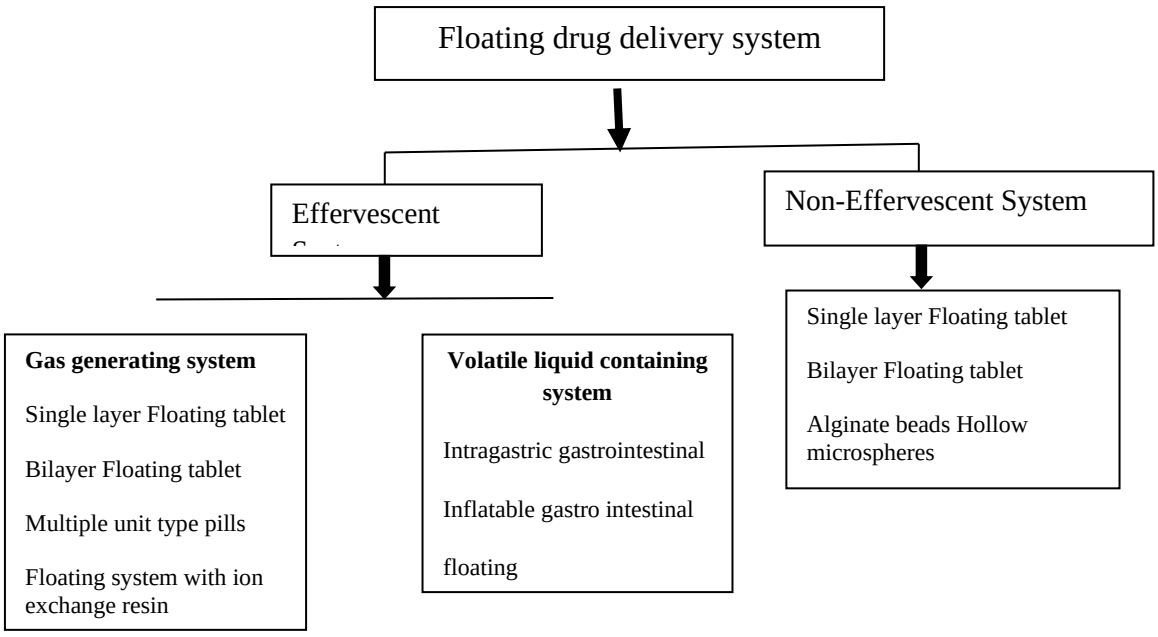
In the Sustained release dosage form, one or more medications are continually released in a predetermined sequence for a set amount of time, either systemically or locally to a specific target organ. It offers more consistent distribution, decreased dosing frequency, less side effects, improved regulation of plasma drug levels, and reduced side effects.[2]

For dosage forms that stay in the stomach longer than conventional dosage forms, the capacity to extend and control the emptying time is a major asset. Gastric emptying of dosage forms is a highly variable process. Currently, a variety of methods are employed to extend stomach retention time. These include delayed gastric emptying devices such as floating drug delivery systems, hydro dynamically balanced systems, swelling and expanding systems, polymeric bioadhesive systems, modified-shape systems, high-density systems, and others.[3]

To keep pharmaceuticals in the stomach, floating drug delivery systems (FDDS) were developed. These devices are useful for medications that have poor intestinal fluid solubility and stability. Making the dosage form less dense than the stomach fluids allows it to float on them, which is the theory behind it.[4] Since it is less dense than gastric fluids; it floats in the stomach for a longer duration without slowing down the gastric emptying rate. [5]

The goal of developing a gastro retentive drug delivery system was to not only sustain drug release but also extend the time that dosage forms remain in the stomach until being released at the right time. The different sphere of beads is a medicine that is coated or enclosed in a microcapsule that serves as the solid substrate for the core of the bead. Beads may have features for controlled release.[6]

Floating drug delivery system is classified as effervescent and non-effervescent system as shown below.[7, 8]



2. Effervescent system

It is a matrix-type system made with the aid of effervescent compounds and swellable polymers like methylcellulose and chitosan. For example, sodium bicarbonate, citric acid, tartaric acid, and These are designed such that when they come into contact with gastric contents, CO_2 is released and held in swelling hydrocolloid, giving the dosage form buoyancy and causing it to float over time.

They are again classified into:

a) Gas generating system

b) Volatile liquid-containing system

a) Gas generating system:

These buoyant systems rely on an effervescent interaction between citric/tartaric acid and carbonate/bicarbonate salts. The system is set up in such a way that when the formulation enters the stomach, carbon dioxide is released, causing it to float there. Other substances, such as a sodium alginate and sodium bicarbonate mixture and floating pills with several units that release carbon dioxide when swallowed, have been described. [9]

b) Volatile liquid-containing system:

A medication delivery system's GRT can be maintained by including an inflatable chamber, which is filled with a liquid, such as ether or cyclopentane that gasifies at body temperature to expand the stomach chamber.[10]

The apparatus may also include a bioerodible plug made of polyvinyl alcohol, polyethylene, or another material that slowly dissolves and causes the inflatable chamber to release gas and collapse after a predetermined period, allowing the inflatable systems to spontaneously eject themselves from the stomach.[11]

3. Non effervescent system

The formulation of non-effervescent FDDS can be accomplished by combining the drug with hydrocolloids that form a gel when in contact with gastric fluid after oral administration and maintain shape integrity and a bulk density barrier. The air trapped by the swollen polymer gives the dosage forms buoyancy.

They are classified into –

a) Colloidal gel barrier systems

b) Microporous Compartment systems

c) Alginate beads

d) Hollow microspheres.

a) Colloidal gel barrier system:

This method comprises medication that forms gels with hydrocolloids and floats on the contents of the stomach. This lengthens the GI stay and improves the Drug is delivered to the site of absorption in solution form, ready for absorption. The hydrocolloid hydrates in the system create a colloidal gel barrier surrounding stomach fluid when in contact with it. The barrier of produced colloidal gel regulates the pace of fluid entry into the apparatus, followed by medication release.[12]

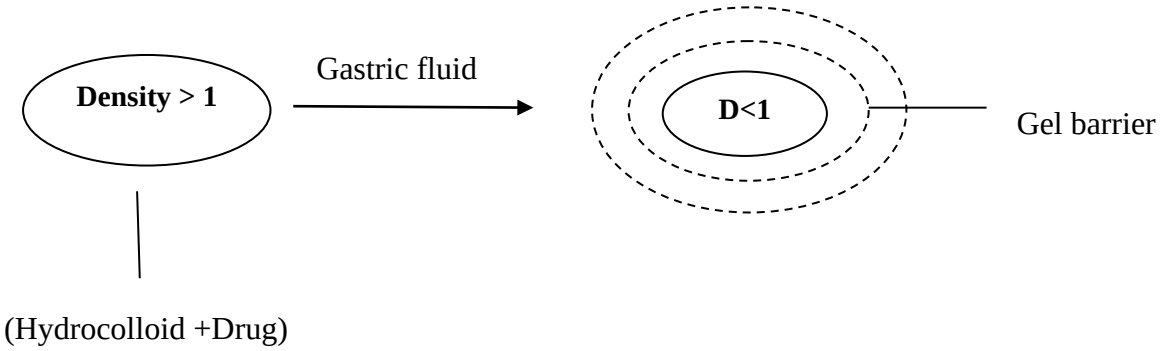


Figure no. 1: Colloidal gel barrier system.

b) Microporous Compartment systems:

A drug reservoir is enclosed in a microporous compartment with pores on the top and bottom of the compartment. To maintain the reservoir compartment's exterior walls were entirely sealed and free of undissolved drugs. New levodopa gastro retentive dosage forms are used that combine extended dimensions with high stiffness. These dosage forms are based on unfolding polymeric membranes.[13]

This method can be used to create huge gelatin capsules. The In vitro unfolded state was obtained within 15 minutes of treatment, according to tests, and it was also confirmed using beagle dogs. The unfolded form was kept in place for at least two hours. It was determined that the treatment of various medications with limited absorption windows might be enhanced by this method.[14]

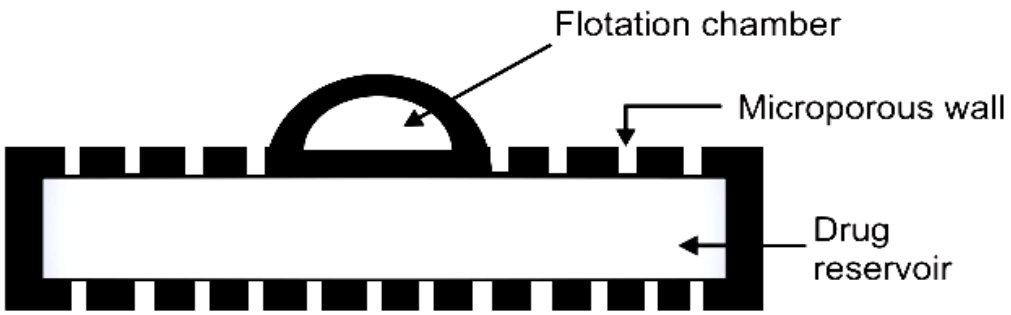


Figure no. 2: Microporous Compartment systems.

c) Hollow microspheres:

Hollow microspheres are non-effervescent gastroretentive drug delivery systems. They are empty spherical particles with no core. They have the distinct advantage of having multiple unit systems, and their center hollow space provides good floating properties, making them promising buoyant systems.[15] These microspheres are free-flowing, low-density powders with a diameter of less than 200 m made of proteins or synthetic polymers. Sustained drug release from buoyant systems improves gastric retention and reduces fluctuations in plasma drug concentration.[16] The number of polymers, plasticizer-polymer ratio, and solvent used in formulation all influence buoyancy and drug release from the dosage form. Polycarbonate, HPMC, cellulose acetate, calcium alginate, Eudragit S, chitosan, and low molecular weight polymers are commonly used to create hollow microspheres. Several studies have shown that hollow microspheres can float continuously over the surface of an acidic dissolution media containing surfactant for more than 12 hours.[17]

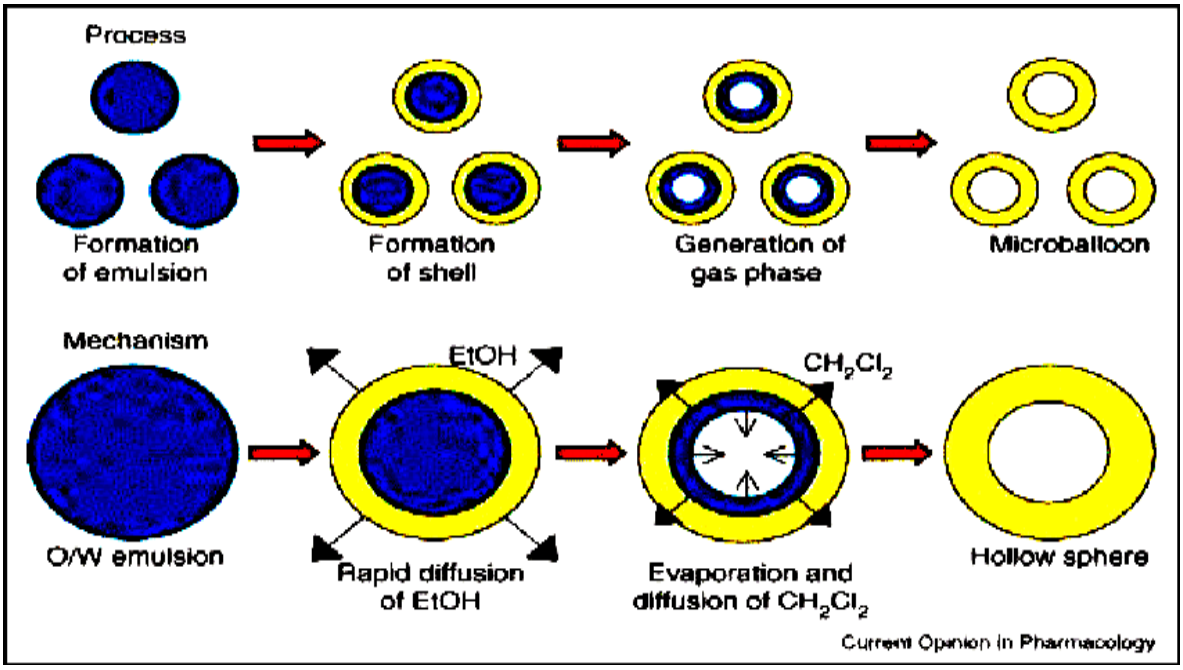


Figure no. 3: Hollow microspheres.

Mechanism of floating drug delivery system

FDDS have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate. After release

of drug, the system is eliminated from the stomach. This results in an increased GRT and a better control of fluctuations in plasma drug concentrations. The floating sustained release dosage forms exhibit most of the characteristics of hydrophilic matrices and are known as 'hydrodynamically balanced systems' (HBS) since they are able to maintain their low apparent density, while the polymer hydrates and builds a gel like barrier at the outer surface. The drug is released progressively from the swollen matrix, as in the case of conventional hydrophilic matrices. These forms are expected to remain buoyant (3–4 h) in the gastric contents without affecting the intrinsic rate of emptying because their bulk density is lower than that of the gastric contents. Many studies have demonstrated the validity of the concept of buoyancy in terms of prolonged GRT of the floating forms, improved bioavailability of drugs and improved effects in clinical situations. The results obtained have also demonstrated that the presence of gastric contents is needed to allow the proper achieve-ment of the buoyancy retention effect. Among the different hydrocolloids recommended for floating form formulations, cellulose ether polymers are the most popular, especially hydroxypropylmethylcellulose(HPMC). Fatty material with a bulk density lower than one may be added to the formulation to decrease the water intake rate and increase buoyancy [18].

In parallel with formulation studies, investigations have been undertaken in animals and humans to evaluatethe intragastric retention performance of coating forms. These assessments were carried out either indirectly through pharmacokinetic studies with a drug tracer, or directly by means of X-ray and gamma scintigraphic monitoring of the transit through the GI tract. When a floating capsule is administered to subjects who have consumed a fat and protein meal, it remains buoyant at the surface of the gastric contents in the upper part of the stomach and moves to the lower region progress-ively as the meal empties from the stomach. The reported gastric retention times range from 4 to 10 h. Pharmacokinetic and bioavailability evaluation studies confirrm the favourable effect of this prolonged gastric residence time. FDDS have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.

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This results in an increased GRT and a better control of fluctuations in plasma drug concentrations.

Because FDDS have a lower bulk density than gastric fluids, they remain buoyant in the stomach for an extended period without affecting the gastric emptying rate.

The drug is slowly released at the desired rate while the system is floating on the gastric contents. The system is eliminated from the stomach after the drug is released.

As a result, GRT is increased and fluctuations in plasma drug concentrations are better controlled.

The floating sustained-release dosage forms are known as "hydrodynamically balanced systems" (HBS) because they can maintain their low apparent density while the polymer hydrates and forms a gel-like barrier at the outer surface. They exhibit the majority of the properties of hydrophilic matrices. The drug is gradually released from the swollen matrix, similar to how it is done with traditional hydrophilic matrices.

Because their bulk density is lower than that of the gastric contents, these forms are expected to remain buoyant in the gastric contents for 3-4 hours without affecting the intrinsic rate of emptying.

Many studies have demonstrated the validity of the buoyancy concept in terms of prolonged GRT of floating forms, improved drug bioavailability, and improved clinical effects.[18]

The obtained results also showed that the buoyancy retention effect cannot be properly achieved without the presence of gastric contents. Cellulose ether polymers, especially hydroxypropylmethylcellulose are the most widely used hydrocolloids among those suggested for floating form formulations (HPMC).

To reduce the water intake rate and increase buoyancy, a fatty material with a bulk density less than one may be added to the formulation.

Parallel to formulation studies, animal and human studies have been conducted to evaluate the intragastric retention performance of floating forms.

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Studies on pharmacokinetics and bioavailability support the beneficial effect of this extended gastric residence time.[19]

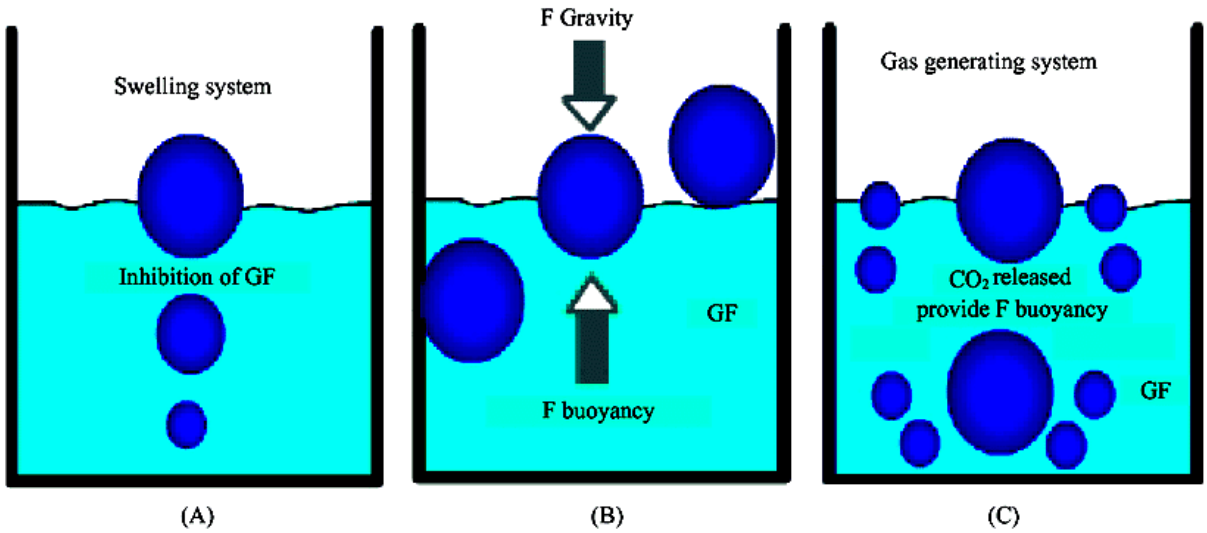


Figure no. 4: Mechanism of floating drug delivery system

Commonly Employed Polymers in Gastro retentive Floating Beads:

Sodium Alginate:

Sodium alginate is a natural polysaccharide as well as an anionic linear polymer with -1, 4-linked L-glucuronic acid and -1, 4-linked D-mannuronic acid residues randomly arranged along the chains. It is a stable gel that contains divalent cations, such as Ca2+, which are used for long-term drug release.[20]

Alginate has high biocompatibility, mucoadhesion, biodegradability, and mild gelation conditions. Alginate beads are also used for floating drug delivery because they are stable in acidic media, preventing drug degradation in the acidic environment of the stomach.[21]

Chitosan:

Ishak RA and colleagues used the ionotropic gelation method to prepare metronidazole (MZ) in chitosan-treated alginate beads by using a factorially designed in which three viscosity-imparting polymers, MC, carbopol 934P, and -carrageenan Two concentrations of chitosan as an encapsulating polymer (0.2 and 0.4% w/v) and two concentrations of low-density magnesium stearate as a floating aid (2.5 and 5% w/w) were tested.[22] Chitosan (HMW) was dissolved in ionic liquid EMIM Ac at B115 1C to make a solution containing 20 mg mL1. At room temperature, the chitosan/EMIM Ac solution was injected into ethanol using a syringe with a 0.33 mm inner-diameter needle. The injection rate was set to 10 ml/h1 and was controlled by a syringe pump (KD Scientific KDS 270, USA). The resulting beads were immersed in ethanol overnight and washed three times to completely remove the ionic liquid. The chitosan beads were then washed three times with water to allow solvent exchange between ethanol and water for 30 minutes. The hydrated chitosan beads were then freeze-dried to produce anhydrous chitosan beads.[23]

Pectin

To form gel particles, an aqueous solution of 6% (w/v) pectin was introduced dropwise by a peristaltic pump through a plastic tubing (0.8 mm inner diameter) into a calcium chloride solution (CaCl 2 6%, w/v). The particles were immersed in a Ca2+ solution for 20 minutes. The beads were then rinsed with distilled water several times until neutral and dried at 37°C.[24]With agitation, pectin was dissolved in water. The solutions (5% w/w) were extruded into 0.34 M calcium chloride with gentle agitation at room temperature using a nozzle with an inner diameter of 0.80 mm. The gel beads were allowed to stand in the solution for 20 minutes before being separated and washed with distilled water. The beads were either air-dried at 37 degrees Celsius for 12 hours or freeze-dried.[25]

Guar gum

For the experiments, 250 milligrams of guar gum were dissolved in 50 mL of distilled water. Guar gum beads were created by syringing guar gum solution into 100 ml of 0.5 M sodium tetraborate solution (pH adjusted to 7.2).[26]

Floating beads can be prepared by:

Emulsion gelation method

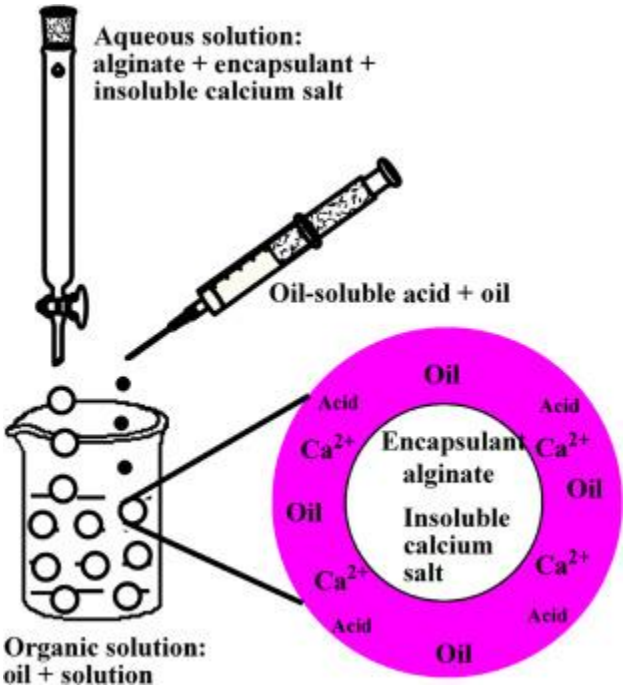
The emulsion gelation method is used to create oil-entrapped gel beads that can float in gastric conditions. Gel beads containing an effervescent agent or edible oil are made by gently mixing or homogenizing an oil phase and a water phase containing pectin or casein, and then extruding into a calcium chloride solution with gentle agitation at room temperature. The prepared gel beads are then separated, washed with distilled water, and dried for 12 hours at 370 degrees Celsius.[27]

Example: oil-entrapped calcium pectinate gel beads.

Ionic Gelation Method

Ionotropic gelation is based on polyelectrolytes' ability to crosslink in the presence of counter ions (Giri et al., 2013d). The ionic gelation method is most commonly used to prepare alginate nanoparticles. Alginate-chitosan nanoparticles were created in two steps, beginning with the ionotropic gelation of polyanion with calcium chloride and ending with polycationic crosslinking (Sarmento et al., 2007). In a gastric pH environment, the nanoparticles retained approximately 50% of the protein for up to 24 hours. Under intestinal pH conditions, the release was close to 75%.

particles were created using a modified emulsification/internal gelation method. This method of preparing alginate nanoparticles does not require any special equipment and can be done at room temperature. The main challenge of this method is the nanoparticle-washing step to remove the residual oil droplets.[28]



Evaluation parameters of floating beads:

Study of size and morphology of emulsion gel beads

A screw gauge was used to determine the diameter of the beads. For this purpose, 20 dried beads were chosen at random from each batch, and the mean diameter was determined using a screw gauge. The smallest screw gauge count was 0.005 mm. Each batch's dried beads were noted for their colour and shape.[29]

DRUG CONTENT:

UV-Spectrophotometry was used to determine the drug content of prepared floating beads.

A precisely weighed quantity of floating beads was taken and dissolved in 100 ml of 0.1N HCl, 1ml of the solution was diluted to 10 ml, and the drug content was estimated using UV at 314nm.[30]

Swelling studies:

Swelling characteristics of beads were investigated. Only Those batches with high drug concentrations were chosen. More than 50% efficiency in content and entrapment. A sample of drug-loaded beads was taken and weighed and inserted into the wire basket of the USP dissolution apparatus II. The basket containing beads was placed in a beaker containing 100

ml 0.1 N HCl (pH 1.2) kept at 370C. The beads were removed at regular intervals. predetermined intervals and weighed.[31]

In vitro drug release studies:

The drug was dissolved in vitro for 300 minutes using a USP Type II dissolution apparatus containing 900 ml of simulated gastric fluid (0,1 N HCl pH 1.2) maintained at 37 0.5°C and speed At 50 rpm, the agitation is strong. Aliquots (5 ml) were collected at regular intervals and replaced with fresh dissolution medium. The collected samples were analyzed with a UV spectrophotometer at a maximum wavelength of 228 nm (UV-1800, Shimadzu). The research was done in triplicate. The percentage of drugs released at different time intervals was calculated and plotted versus time.[32]

CONCLUSION:

Formulation of FDDS is an efficient and potential approach for gastric retention of dosage forms to improve bioavailability and also to achieve controlled release of dosage form. The most important criteria which has to be looked into for the formulation of a FDDS is that the density of the dosage form should be less than that of gastric fluid by this method we can thus reduce the dosing frequency and improve patient compliance. In this review, we discussed in details regarding floating drug delivery system, its classification and its mechanism, commonly employed polymers in gastro retentive floating beads, methods of preparation and evaluation of floating beads.

ACKNOWLEDGEMENT:

The author is grateful to thanks the management of SJM College of Pharmacy for their continuous support.

CONFLICTS OF INTEREST:

The authors declare that there is no conflict of interest.

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