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A REVIEW ON FLOATING DRUG DELIVERY SYSTEMS

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Abstract:

The principle behind writing this review on the floating drug delivery system (FDDS) had as its main goal organizing the latest research on the fundamental role that flotation plays in gaining gastric retention. The buoyancy mechanism serves as the foundation for the various techniques utilized in the development of FDDS, including the construction of both effervescent and non-effervescent floating tablets. Drugs that are unstable in the lower intestine environment, have a limited window of absorption in the upper gastrointestinal system, and are poorly soluble at higher pH levels can be delivered via the FDDS technique. Among the innovative techniques in FDDS are methods for designing floating systems with one or more units. The design of single- and multi-unit floating systems, the physiological and formulation variability influencing stomach retention, and the application of recently created and produced polymers are some of the novel methodology in FDDS. In light of the functionality and applications of floating systems, this review also emphasizes a variety of in vitro methods and in vivo investigations. In addition to the gas-generating agent, appropriate components can be added to tablets or capsules to create floating dosage forms that can be administered conventionally.

Keywords — FDDS, gastric retention, buoyancy, gas-generating agent, effervescent tablets.

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I. INTRODUCTION

One type of gastro retentive medication administration technique is the floating tablet. By lengthening the duration that dosage forms remain in the stomach, gastro retentive systems can improve the bioavailability of medications with a limited window for absorption, less water solubility in the small intestine's alkaline pH, or poor stability in the intestinal or colonic environment. When developing oral controlled release dosage forms, it's crucial to consider not only how long the drug will stay in the stomach or upper gastrointestinal system after it is delivered—this ensures that the drug is released for the desired amount of time. Fast gastrointestinal transit may cause partial drug release from the drug delivery device in the absorption zone, which would reduce the dose's effectiveness. Maintaining the drug reservoir above its absorption area—the stomach—and releasing the drug in a controlled manner to achieve zero order kinetics for an extended period of time is a sensible strategy to improve bioavailability and pharmacokinetic and pharmacodynamic profile. One of the most practical strategies for achieving a prolonged and predictable drug delivery profile is to control the gastric residence time in the GIT[1].

II. CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM

(A) Effervescent FDDS

1. Gas generating system.

2. Volatile liquid containing system

(B) Non – Effervescent FDDS

1. Colloidal gel barrier system.

2. Microporous compartment system

3. Floating microspheres / micro balloons

4. Alginate floating beads9.

(C)Raft forming system

(A)**Effervescent system:** Effervescent systems include use of gas generating agents, carbonates (e.g Na bicarbonate) and alternative organic acid (e.g acid and salt acid) gift within the formulation to supply CO2 gas so reducing the density of system and creating it float on the gastric fluid. an alternate the incorporation of matrix containing portion of liquid that manufacture gas that evaporate at body temperature[2]

1. **Gas generating systems:** These are formulated by intimately mixing the CO2 generating agents and the drug within the matrix tablet. These have a bulk density lower than gastric fluids and therefore remain floating in the stomach unflattering the gastric emptying rate for a prolonged period.

2. **Volatile liquid vacuum containing systems**: This system is created to float within the abdomen owing to floatation chamber which can be a vacuum or full of air or a harmless gas, whereas drug reservoir is encapsulated within a micro porous compartment.

(B) **Non- Effervescent system**: This type of system when swallowing swell unrestrained via inhibitions of viscous fluid to associate extent that it prevents their exit from the abdomen. These systems could also be remarked because the plug type system since they need a bent to stay lodged close to pyloric valve. One in all formulation strategies of such indefinite quantity forms involves the blending of drug with a gel that swells involved with viscous fluid when oral administration and maintains a relative integrity of form and a bulk density of but one inside the outer jelly like barrier. The air at bay by the swollen compound confers buoyancy to the current indefinite quantity forms. The foremost normally used excipient is non effervescent floating drug delivery system area unit gel forming or extremely swells able polysaccharide sort hydrocolloids, polysaccharides and matrix forming polymers like polyacrylate, polymethacrylate and polycarbonate.

1. **Colloidal gel barrier systems (hydrodynamic balanced system):** This system prolongs gastric retention time and maximizes the amount of drug that reaches its absorption site in the solution form. It essentially contains drug with gel –forming hydrocolloids to remain buoyant on the stomach content. Such as polycarbophil, polystyrene and polyacrylate. Upon contact with gastro intestinal fluid the hydrocolloid in the system hydrates to generate a colloid gel barrier to its surrounding.

2. **Micro porous compartment systems:** This technology incorporates the encapsulation technique of a drug reservoir inside a micro porous compartment along with pores at top and bottom walls. In the stomach the floatation chamber composed of entrapped air causes the delivery system to float over the gastric content[3].

1. **Floating Microspheres / Micro balloons:** Hallow microspheres also are known as micro balloons are considered as a most efficient buoyant system. It is composed of central hallow space inside the microsphere. Hallow microsphere is loaded with a drug in their outer polymer shelf are fabricated by a novel solvent diffusion method for emulsion.

2. **Alginate beads / Floating beads:** Multi – unit floating dosage forms have been developed from calcium alginate spherical beads of about 2.5 mm in diameter and can be fabricated by adding sodium alginate solution into aqueous solution of calcium chloride, resulting in the precipitation of calcium alginate, the beads are further separated, snap – frozen in liquid nitrogen and freeze – dried at 400˚c for 24 hrs leads to generation of a porous system. this fabricated system would maintain a floating force for over 12hrs and these floating beads

provide a longer residence time of more than 5.5 hrs.

(C) **Raft- forming systems:** Raft – forming system are in much attention for the delivery of antacid and drug delivery for gastro infection and disorders. On contact with gastric fluid, a gel – forming solution swells and forms a viscous of gastric fluid thus facilities release drug slowly in the stomach[4].

GIT physiology

The term "human gastrointestinal tract" usually refers to the stomach and intestines, but it can also apply to the entire system, including the mouth and the anus. The Gastrointestinal (GI) tract measures 5 meters (20 feet) in length in an adult male person. The oesophagus, stomach and duodenum make comprise the upper digestive system. Muscle tone, and consists of the upper and lower GI tracts. Some sources additionally mention the mouth cavity and pharynx. Foregut, midgut and hindgut are additional classifications for the tract that reflect the embryological origin of each section. To help control the digesting process, the GI tract releases hormones. Gastrin, secretin, cholecystokinin and grehlin are just a few of the hormones that are mediated by either intra or auto crine pathways, showing that the cells that release these hormones have remained relatively constant over the course of evolution. The precise line between "higher" and "lower" can differ. The duodenum may appear to be a single organ upon gross dissection; however it is frequently divided into two portions based on function, vascular supply, or embryology[5].

Advantages of floating drug delivery system Floating dosage systems are delivery systems with gastric retentive behavior and offer several advantages in drug delivery. Some of these include:

1. A straightforward and traditional formulation method.

2. Delivery of drugs to particular sites.

3. Medication delivery under control.

4. Administration of medication for lingering effects at a particular stomach location.

5. Better drug absorption with higher GRT and longer dose regimen contact times at the intended location.

6. Reducing the amount that medications with a slow release rate irritate the GIT mucosa.

The floating medicine delivery system's drawbacks:

1. The main drawback of a floating system is the requirement for an adequate amount of stomach contents in order to float without the aid of a sink.
2. This restriction can be addressed, though, by covering the dose form in bioadhesive polymers, which cling to the stomach mucosa with ease.
3. The majority of desirable candidates are those medications that have significant first-pass metabolism and are greatly absorbed throughout the gastrointestinal tract.
4. Some medications included in the floating system may irritate the mucosal linings of the stomach.
5. The rate at which the stomach of a floating system empties varies greatly depending on its dimensions. Consequently, patients shouldn't take their medication right before bed[6].

Selection criteria of drugs for the floating drug delivery system:

1. Easy absorption through the upper digestive system.
2. Substances that have a low pKa but do show unionized characteristics.
3. Drugs become less soluble at higher pH values.
4. The impact of medications' local actions, such as treating *Helicobacter pylori* in ulcerative situations.

5. Drugs that break down in alkaline pH circumstances can have their bioavailability increased by being manufactured into forms that are gastro retentive[7].

III MATERIALS AND METHODS

I. Floating tablets were prepared by the wet granulation method by using hydroxyl propyl methyl cellulose (HPMC K4MCR), carbopol 934P, lactose and sodium bicarbonate.

Preparation of granules:- Granules were made using the wet granulation technique. Every ingredient was precisely weighed. The medication, lactose, sodium bicarbonate, and HPMC-K4MCR were then precisely weighed and homogeneously blended using a glass mortar and pestle. Ninety-five percent ethanol was used for the wet granulation. The wet bulk was dried overnight at 40°C in a hot air oven after being run through a 40-mesh screen. The dried granules were combined with approximately 1% w/w of magnesium stearate after being sized through a 40/60 mesh screen. Lactose served as a channeling and filling agent. Here, ethanol serves as the granulating agent while sodium bicarbonate is utilized as a gas-generating agent[8].

Preparation of floating tablet:- The homogeneously lubricated granules with magnesium stearate (1% w/w) were then compressed in to tablet using single punch tablet compression machine. Compression force was adjusted to obtain tablet with hardness in the range of 6.2-6.9 kg/cm^2 on a Monsanto tablet hardness tester. Floating tablets can be prepared by direct compression method. Here pure drug was mixed with required quantity of HPMC K4M, sodium CMC, carbopol 934P, sodiumbicarbonate and lactose by geometric mixing in mortar and pestle for 10 min. The above powder was lubricated with magnesium stearate in mortar and pestle for 2min. The lubricated blend was compressed into tablets using rotary tablet machine[9].

The dry granulation method (slugging method): The ingredients in the formulation are mixed properly and precompressed on rotary tablet machines. The slug which is formed is ground to a uniform size and compressed into the finished tablet [10].

EVALUATION OF FLOATING TABLETS:

- **Bulk density:** It is a ratio of mass of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder was carefully poured in to graduated measuring cylinder through large funnel and volume was measured, which is called initial bulk volume. It is expressed in gm/ml and is given by the formula:

Bulk density=M/Vo; Where, M = mass of the powder; Vo = bulk volume of the powder.

- **Tapped density:** 10 gm of powder was introduced into a clean, dry 100 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. It is expressed in gm/ml and is given by:

Tapped density=M/Vt Where, M = mass of the powder; Vt = final tapping volume of the powder.

- **Angle of repose (θ):** It is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at a given height 'h, above a flat horizontal surface to which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of the funnel. The angle of repose was then calculated using following equation:

Angle of repose Ø = tan1(h/r) Where, h=height of the pile; r=radius of the pile.

- **Compressibilty Index (carr's Index):** Compressibilty Index is used as an important parameter to determine the flow behavior of the powder. It is indirectly related to the relative flow property rate, cohesiveness and particle size. It is simple, fast and popular method for predicting flow characteristic. Carr's index can be represented by equation:

- **Hausner's ratio:** Hausner's ratio is used to predict the flowability of the powders. This method is similar to compressibility index. Hausner's ratio can be represented by equation:

Hausner's ratio = Tapped density / bulk density

- **Floating lag time and total floating time:** Floating lag time (FLT) and total floating time (TFT) of floating tablets were measured visually in dissolution apparatus type II containing100 mL 0.1 N HCl with a paddle rotated at 50 rpm (pH 1.2) at 37 ± 0.5 °C.
- **Swelling index:** The prepared tablets were placed in a glass containing 200 ml of 0.1 N HCl at 37 ± 0.5°C. The percentage of swelling at different time interval was calculated by the following equation. Where, SI is swelling index, Wt is weight of tablet at time t, Wo is weight of the dry tablet before placing in the glass.
- **Dissolution Study:** In vitro drug release of the formulation was carried out using USP dissolution apparatus type II paddle type under sink condition with rotating speed of 50 rpm and at temperature of 37 ± 0.5 °C. The dissolution medium used was 900ml 0.1NHCl. The samples were withdrawn at predetermined time intervals for period of 6hours and replaced with the fresh medium, suitably diluted and were analyzed using UV/Visible spectrophotometer.
- **Dimensional Analysis:** The thickness and diameter of tablets was determined using vernier calipers. Twenty tablets from each batch were used and average values were calculated.
- **Hardness:** Tablet hardness and strength are the essential to see that the tablet can with the shock and stress during manufacturing packing and transportation, and while handled by the patient. To test the hardness of the tablet Monsanto tester, Strong-cobb tester, the Pfizer tester, the Erweka tester, the Schleuniger testers are used.
- **Friability:** Friability is the tested for a tablet to see whether the tablet is stable to abrasion or not, it is tested by using Roche friabilator. This is made up of a plastic drum fixed with a machine which rotated at 25 rpm for 100 revolutions. And then the twenty tablets which were weighed prior to the test are taken out of the drum and cleaned with a cloth and weighed once again, the weight variation must not be less than 0.5 to 1.0% for an conventional tablet.
- **Size and Shape:** It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micrometer or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value.
- **Weight Variation test (U.S.P.):** Take 20 tablets and weighed individually. Calculate average weight and compare the individual tablet weight to the average. The tablet pass the U.S.P. test if no more that 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.
- **Disintegration Test (U.S.P.):** The U.S.P. device to test disintegration uses 6 glass tubes that are 3" long; open at the top and 10 mesh screens at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 2 0 C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass.

Disintegration time: Uncoated tablet: 5-30 minutes coated tablet: 1-2 hours[12].

Mechanism of floating drug delivery systems

Several attempts have been made to maintain the dosage form in the stomach in order to extend the retention period. The use of floating, mucoadhesive, high-density, modified, and gastric-emptying delaying devices, as well as the co-administration of drugs that delay gastric emptying, are some of these endeavors. The dosage forms that are used most frequently are the floating ones. Gastric fluids float in the stomach without slowing down the rate of stomach emptying because they have a lower bulk density than Floating Drug Delivery Systems (FDDS). The medication floats on the contents of the stomach and is gradually removed from the

system at the desired rate. After release, the drug's residual system is eliminated from the stomach[13]. Consequently, GRT increases and the fluctuations in plasma drug concentration are more effectively controlled. However, in addition to the minimal stomach content required to allow the successful accomplishment of the buoyancy retention effect, a minimal level of floating Force (F) is also required to maintain the buoyancy of the dosage form on the surface of the meal. The literature has detailed a novel device for measuring the dynamics of the floating force and computing the resulting weight. The mechanism of the apparatus involves the continuous measurement of the force F (as a function of time) required to maintain an object submerged[14].

III. CONCLUSIONS

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[15]. And therefore, it is concluded that these dosage forms serve the most effective in the treatment of diseases associated with the GIT and for extracting a prolonged action from a drug with a short half-life. Inspite of number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing towards commercializing this technique. Number of economic products and patents issued in this field are evident of it.

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REFERENCES

[1] J. Dubey, N. Verma. *Floating Drug Delivery System: A Review*, IJPSR, 2013; 4(8):2893-2899.
[2] 2) Baviskar P, Patil P, Saudagar RB, Floating Drug Delivery System: A Comprehensive review, Journal of drug delivery and therapeutics, 2019; 9(3-s): 839-846.
[3] 3) Sharma AR, Khan A, Gastroretentive drug delivery system: An apporch to enchance gastric retention for prolonged drug release, IJPSR, 2014; 5(4):1095-1106.
[4] 4) Ninan S, John Wesley I, Kumaran J, Aparna P, Jaghatha T, A Review on Floating Drug Delivery System, Wjpmr, 2018; 4(5):275-281.
[5] 5) Vedha Hari B.N.et al, The Recent Developments on Gastric Floating Drug Delivery Systems: An overview, Int .J. PharmTech Res, 2010; 2(1):524-534.
[6] 6) Kotreka UK, Adeyeye MC, Gastroretentive Floating DrugDelivery Systems: A Critical Review, Critical ReviewsTM in Therapeutic Drug Carrier Systems, 2011; 28(1):47-99.
[7] 7) Kumar N, Niranjan SK, Irchhaiya R, Verma V, Kumar V, Novel Approches of Floating Drug Delivery Systems: A Review, IJPRS, 2012; 1(4):96-111.
[8] 8) S .T. Deshpande et al, Floating Drug Delivery System: A Novel Approach towords Gastroretentive Drug Delivery System, Research J. Pharma. Dosage Forms and Tech, 2013, 5(4); 191- 201.
[9] 9) Pakhale NV, Gondkar SB, Saudagar RB, Effervescent Floating Drug Delivery System: A Review, Journal of Drug Delivery and Therapeutics. 2019; 9(3-s):836-838.
[10] 10) Singh LP et al, Floating effervescent Tablet: A Review, JPBMS, 2011; 5(11):1-6.
[11] 11) Pawar VK, Shaswat K, Garg G, Awasthi R, Singodia D, Kulkarni GT, Gastroretentive Dosage Forms: A review with special emphasis on floating drug delivery systems, Drug Delivery, 2011; 18(2):97-110.
[12] 12) Padhan et al, Floating Oral In-situ Gel, A Comprehensive Approach of Gastroretentive Drug Delivery System: A Review, IJPSR, 2019; 10(9):4026-4039.
[13] 13) Chowdary KPR, Shankar KR, Teeda V, Floating Drug Delivery Systems: A Review of Recent Research, IRJPAS, 2014; 4(4):14- 24.
[14] 14) Grover I, Marwah M, Devgan M, Floating Drug Delivery systems: A Novel Approach, Research J. Pharm. and Tech. 2015, 8(4); 490-495.
[15] 15) A Bhosale Aishwarya Rajendra*, Shinde Jitendra V., Chavan Rajashree S. Comprehensive Review on Floating Drug Delivery System (FDDS). Journal of Drug Delivery & Therapeutics. 2020; 10(6):174-182

