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AN UPDATE REVIEW OF FLOATING DRUG DELIVERY SYSTEM

Sarvan*

Research Scholar, HIMT College of Pharmacy, 8 Institutional Area, Knowledge Park-1, Greater Noida, Uttar Pradesh – 201301.

***Corresponding Author: Sarvan**

Research Scholar, HIMT College of Pharmacy, 8 Institutional Area, Knowledge Park-1, Greater Noida, Uttar Pradesh – 201301.

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ABSTRACT

The primary goal of that article's work on floating drug delivery systems (FDDS) is to assemble a report on recent investigations and analyses with a focus on the fundamental flotation mechanism for internal organ retention. By conquering physiological challenges, such as short stomach residence periods and sudden internal organ evacuation periods, rate-controlled oral medication delivery systems have made significant scientific and technological advances in recent years. This evaluation served as an example of how to use in vivo testing to evaluate the development and use of floating systems as well as their applications. These methods are beneficial for various inquiries regarding the event of a pharmaceutical dose type.

KEYWORDS: Floating Drug Delivery System (FDDS), Gastric Retention Time, Floating Tablet, Evaluation, Methods, FDDS Application.

INTRODUCTION

The oral route of medication administration is the simplest method of drug delivery, and patients also find this route to be quite comfortable. Even though oral drug delivery is extremely rarely used for several significant medications from different pharmacological classes, some medications have very low bioavailability due to poor digestion and imprecise absorption. Some of these medications can be identified by their narrow absorption window (NAW) at the top of the alimentary canal, which displays their extended absorption capabilities when compared to the nearby area of the small intestine. Use frequent medication administration and remove medications from the bloodstream as soon as possible. The oral controlled release drug delivery system is used in an investigation to release the drug slowly into the GI tract and maintain a persistent drug concentration in the blood for a longer period of time in order to avoid these issues. Extending gastric retention, which is crucial to managing GRT, enables the stomach to hang on to the controlled drug release mechanism for a longer time and in an anticipated manner.[1] Due to its lower density than gastric fluid, the preparation floats in the stomach's contents. A floating system composed of several establishment forms has achieved benefits alignment to a straightforward unit preparation next to a distinct formulation. The three components of the methodology—physiochemistry, drug attribute,[2] anatomy and physiology of the alimentary canal, and dose form.[3] are vital to the preferred circumstances of oral controlled drug delivery systems.

Floating Drug Delivery Systems

Low-density systems having sufficient buoyancy to float over the contents of the stomach and remain buoyant there without significantly slowing down the rate at which the stomach empties its contents are known as floating systems or hydrodynamically regulated systems. As a result, the stomach retention duration is prolonged, and the fluctuations in plasma drug concentration are better managed.[6]

In the stomach, that is locally active. have a window for absorption in the small intestine. That is unstable in an environment such as the colon or intestines. At high pH values, they have little solubility.

Physiology of the Gastrointestinal Tract

The abdomen's primary function is to store and move food through the digestive system. The abdomen is a stomachic organ located between the small intestine and the oesophagus. The structure of the stomach is shaped like a "J." The stomach is anatomically divided into four main parts: the aperture, fundus, body, and pylorus. The front and posterior sides are fluently orbicular, and a serous membrane surrounds the stomach.

Cardia: The stomach region closest to the oesophagus. Food and liquids enter the stomach via the cardia from the oesophagus.

Fundus: The fundus is part of the stomach that stores gas from digestion.

Body: It is located close to the fundus. The body is the large median portion of the stomach.

Pylorus: The pylorus is a valve that opens and closes during digestion. This allows partially digested food and other stomach contents to pass from the stomach to the small intestine.[5]

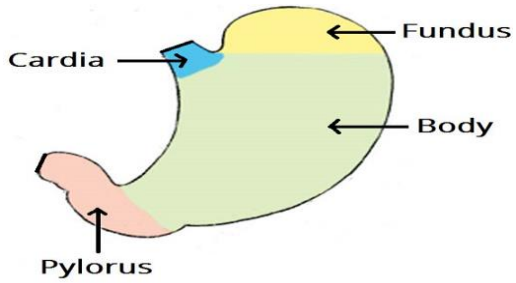

Fig. 1: Structure of GIT.

Whether you are eating or not, your stomach empties both ways. However, the two states, as well as the motility pattern, differ from one another. An inter-digestive series of electrical events occur during the fasting state and cycle through the stomach and intestine every two to three hours.[8] The term for this occurrence is the inter-diastolic myoelectric cycle (IDMC) or migrating myoelectric cycle (MMC), which is further broken down into the following 4 phases as defined by Wilson and Washington.[8] The following details about the 4 phases are explained below:

Stage I: In the basal phase, contractions are infrequent and persist for 40 to 60 minutes.

Stage II: (The pre-burst phase) is forty to sixty minutes long with sporadic contractions and action potential. progressive increases in both power and frequency rise throughout the phase as well.

Stage III: (The burst phase) lasts between four and six minutes. It contains brief, recurring contractions that are strong and frequent. All of the undigested material is pushed out of the stomach and into the small intestine as a result of this wave. Another name for it is the "housekeeping wave."

Stage IV: Between stages III and I of two consecutive cycles, lasting 0–5 minutes. The pattern of contractions switches from that of a fasted state to that of a fed state following the consumption of a mixed meal. In phase II of the fasting state, constant contractions are present in this pattern, which is also known as the digestive motility pattern.

Fdds-Compatible Drug Candidates

Drugs with a limited window of absorption in the GIT, such as riboflavin, aminobenzoic acid, furosemide, and Levo dopa.[9] Antacids and misoprostol are two medications with a specific impact on the stomach.[10] Drugs that are unstable in the intestinal or colonic environment, such as metronidazole, ranitidine HCl, and captopril.[11] Drugs that disrupt the natural colonic flora, such as antibiotics used to treat Helicobacter pylori,[12] such as tetracycline as well as amoxicillin, Verapamil, chlordiazepoxide, and diazepam, for example, are poorly soluble when the pH is high.[13]

Classification of Fdds

A. Floating Systems for One Unit

a) Systems with Effervescence

b) Systems Without Effervescence

B. Floating Dosage System With Multiple Units

a) Systems with Effervescence

b) System Without Effervescence

c) Microspheres with Holes

C. System for Forming Raft

A) Floating Systems for One Unit

Individual-dose formulations are easier to create. However, because they totally or completely fail to empty, they could lose their impact too soon after entering the stomach. As a result, they can have a high degree of bioavailability variability and can cause local discomfort because a significant amount of the medication is administered at one particular site in the digestive system.

a) Systems With Effervescence

These are systems that resemble matrices that are made with fizzy substances, including tartaric acid, citric acid, and sodium bicarbonate, along with numerous Chitosan and methylcellulose are two elastomeric polymers. They are designed such that hydrocolloids swell when CO2 comes into contact with the acidic contents of the stomach, giving the dosage buoyancy.

b) Systems Without Effervescence

The following are used: hydrocolloids, polysaccharides, and matrix-forming polymers such polyacrylate, polycarbonate, polystyrene, and polymethyl methacrylate to form cellulose that gels or swells in non-effervescent floating dose forms. The formulation technique entails mixing the hydrocolloid-forming gel and medication thoroughly using a simple procedure. This dosage form swells after being given by mouth and reaches a bulk density of <1. The buoyancy of the dosage shape is provided by the trapped air within the swollen matrix. This results in the formation of a swollen, gel-like substance that serves as reservoir, allowing the gelatinous mass to release the medication in a sustained manner. The most common excipients employed in these systems consist of hydroxypropyl methyl cellulose (M.C), polyacrylate polymers(P.P), calcium chloride (C.C), polyvinyl acetate (P.A), polyethylene oxide (P.O), sodium alginate (S.A), Carbopol, polycarbonate, and agar.[14]

B. Floating Dosage System With Multiple Units

Many forms of dose units may be an attractive alternative because it has been established that the risk of dose dumping is decreased, as are internal and external subject variations in drug assimilation. A number of floating systems with multiple units were developed

using concepts such as an air compartment multiple unit system, hollow microspheres prepared using the emulsion solvent diffusion method, and beads prepared using the emulsion gelation process. The use of effervescent and water-swellable polymers is another technique for planning multiple-unit FDDS.

a) Systems With Effervescence

A multi-unit system with a calcium alginate/PVA and a calcium alginate core separated by an air compartment was developed. In the presence of water, the PVA leaches out and increases the permeability of the membrane, preserving the integrity of the air compartment. The system's floating properties have improved as the PVA concentration and molecular weight have increased.[15]

b) Systems Without Effervescence

In comparison to systems that effervesce, In the literature, there wasn't much information about effervescence numerous unit systems. However, few academics have documented the possibility of appearing a drug that contains using chitosan to administer indomethacin as a polymer excipient. A good drug made by utilising the extrusion method uses an indomethacin-containing multiple HBS unit. The extrudate is transparent and cut after being cut by a blade that extrudes a mixture of chitosan, acetic acid, and prescription. Required drug release in acidic media, chitosan hydrates, and flocs could be achieved by changing the drug-polymer ratio.[16]

c) Microspheres with Holes

Using a novel technique called emulsion solvent diffusion, empty microspheres loaded with drugs were produced in their exterior polymer shelf. Enteric acrylic polymer and the drug's ethanol/dichloromethane solution were added to a thermally regulated, agitated polyvinyl alcohol solution at 400 degrees Celsius. The gaseous phase is resulting from the dichloromethane's evaporation formed in the drug polymer microsphere's internal cavity and the dispersed polymer droplet. The tiny balloon floated without stopping over an acidic dissolving medium's surfactant surface for more than 12 hours. Because of the empty core section of the microsphere, one of most promising buoyant structures are hollow microspheres because they have enhanced floating properties in addition to the special benefits of several unit systems.[17]

C. System for Forming Raft

When a gel-forming liquid, such as stomach juice containing trapped CO2 bubbles, comes into contact with bicarbonate and carbonate, both of which contain alginate sodium solution, it expands, forming a cohesive, thick gel. To reduce gastric acidity, antacids like calcium carbonate or aluminium hydroxide are commonly used in formulations. Because raft-forming systems form a coating on top of gastric fluids, they are also used to treat gastroesophageal reflux. When a slick, cohesive gel comes into touch with stomach fluid, the liquid expands in each region to make a layer that is continuous that is known as a raft. Here one of the techniques for raft creation. Because of its low density and carbon dioxide generation, this raft floats on abdomen acids.[18]

Polymers Are Used In A Floating Drug Delivery System (FDDS)

Polyvinyl alcohol, Polycarbonate, Chitosan, Eudragit, Casein, Cellulose acetate, Sodium alginate.[19]

Table 1: Marketed Drug Used In Floating Drug Delivery System (FDDS).

DRUG NAME	DOSAGE FORM	BRAND NAME	MANUFACTURER
Ofloxacin	Tablet	Oflin O. D	Ranbaxy, India
Misoprostol	Capsule	Cyto Tech	Pharmacia, USA
Diazepam	Capsule	Val Release	Hoffmann-La, Roche USA
Metformin Hcl	Tablet	Glumetza	Roche, India
Benserazide	Capsule	Madopar HBS	Roche, India
Ciprofloxacin	Tablet	Cifran O. D	Ranbaxy, India
Ferrous Sulphate	Colloidal Forming FDDS	Ferro Care	Ranbaxy, India

Table 2: Frequently Used Drugs In the Production Of Gastro-Retentive Dosage Form.

S.NO.	DOSAGE FORM	DRUG USED
1	Floatable Microspheres	Aspirin, Ibuprofen, Terfenadine, Griseofulvin
2	Floatable Granules	Diclofenac sodium, Prednisolone & Indomethacin
3	Floatable Capsule	Diazepam, Furosemide, Misoprostol, Benserazide and L-Dopa
4	Floatable Tablet & Pills	Ampicillin, Amoxicillin, Atenolol, Diltiazem, Fluorouracil, etc

Mechanism of Floating Drug Delivery System

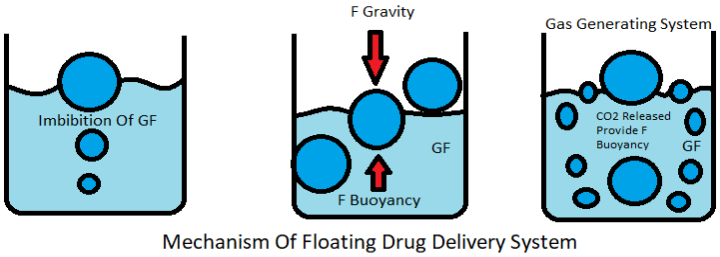

Fig. 2: Mechanism of FDDS.

In the stomach, FDDS float for a long time without reducing the stomach emptying rate since they are less dense in volume than gastric fluid. When the gastric contents are floating, drugs are released from the body at the appropriate rate. An absolute minimum of force (F) in floating is necessary to maintain floating particles over the meal's surface. A new technique is used to calculate the floating force kinetics for calculating the weight, as documented in the literature. The device works by continually monitoring the force, which is equal to F, required to support the submerged object.[32]

This technology aids in the optimization of floating drug delivery systems with relation to the stability and longevity of the floating forces created, thereby avoiding the drawbacks of unanticipated changes in the performance of intragastric buoyancy. As the drug is dissolving in the stomach's contents, it is removed slowly and at the ideal pace from the system.[33]

METHODS OF PREPARATION

I) Evaporation of solvent

A dose form with floating multiple particles was made using diffusion and evaporation of solvents techniques to produce an interior empty core. The drug is disintegrated in the polymer's organic solution after the polymer is dissolved in an organic solvent.

To make an O/W emulsion, polyvinyl alcohol is present in the aqueous phase that results from the emulsion of the drug solution. After that, The organic solvent is removed by swirling constantly or by raising the temperature.

When the evaporator is withdrawn, the polymeric precipitates at the droplet interface, hollowing out the gouttes and forming a cavity that allows them to float. Acrycoat, polyvinyl acetate, Chitosan, Eudragit, Carbopol, Methocel, Polyacrylates, and Agar is one of the polymers under consideration for these kinds of flotation systems.

Theophylline floating particles were created using an O/W solvent evaporation process and powdered polypropylene foam, ethyl cellulose, Eudragit RS 100, or polymethyl methacrylate. For dissolving the drug and rate-regulating polymer, methylene chloride was used. Poly-propylene powder was then given out throughout the prepared phase of organic matter. In a polyvinyl alcohol aqueous solution, the final suspension was blended. The large particles were straining, cleaned in lukewarm water, and then dehydrated in a desiccator using adequate silicas gel, they all have a porous structure and are uneven in size and shape.

Overall efficiency of drug cojoining was high and essentially unaffected by the method's assumed drug loading. The formulation evaluation will yield a variety of drug release schedules. This novel preparation approach has several advantages, including a short time for preparation, no product exposure to extreme heat, a proclivity for avoiding harmful chemical solvents, and maximisation of medicine combination effectiveness.

The floating particle framework is made of powdered polymer foam, a good drug like polymethyl methacrylate, and chlorpheniramine maleate. Microporous foam molecules were soaked in an organic solution containing drugs and the polymer. Microparticles with a low density can also be compacted into quickly dissolving capsules, producing an oral dosage type that is simple to administer.

II) Method of Ionotropic Gelation

Ionotropic gelation occurs when polyelectrolytes cross-connect in the presence of counterions, resulting in the development of beads. Since the application of gellan gum, chitosan, alginates, & CMC for drug synthesis, this solidification or gelation method has been commonly employed to make beads.

With these anions form a mesh like structure and add gelation by predominantly merging using anion blocks. when combined with polyvalent cations. Hydrogel beads are formed when a drug-loaded polymer solution is poured into water-based polyvalent cationic solution. Biological molecules can be introduced under light conditions to maintain the three-dimensional structure of these beads.

III) Diffusion technique of emulsion solvent

A novel emulsion solvent diffusion procedure was used to manufacture micro-balloons that contained drugs within the outer polymer shells. Drug solution & polymer in Methylene chloride with ethanol are poured into a diluted vinyl alcohol aqueous polymer solution.

Methylene chloride that is trapped evaporatively, causing internal cavities to form within the microparticles.[20]

Analysis Of Floating Drugs Delivery Systems (FDDS)

1. Measurement of tablet hardness

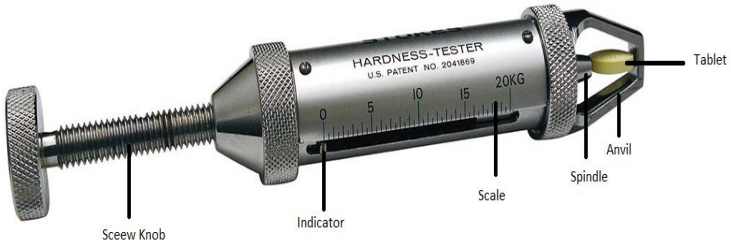

Fig. 3: Structure of Monsanto.

A random sample of twenty tablets from each formulation batch should be used to determine hardness using a Monsanto-type hardness tester.[21]

2. Measurement of weight variation

Twenty tablets are chosen at random, and their average weight is calculated. Following that, the individual weight variation from the average weight is computed.

3. Measurement of the tablet's thickness

For each batch, the distinct individual from crown to crown broadness of 10 tablets is measured with a vernier caliper.[22]

4. Floating lag time

It is the amount of time it takes for the tablet to emerge on the surface of the dissolution medium, indicated in seconds or minutes.[23]

5. Measurement of Floating Capacity

Three separate tablets are placed in each flask, which contains 400 mL of 0.1N HCL solutions. The duration of floating and the floating lag time, which are both measured in minutes, are the amount of time that it takes for a tablet to consistently float on the water's surface. Following that, the sample means and standard deviation are computed.[24]

6. Angle of repose

Angle of repose is a useful tool for quantifying frictional forces in loose powder. The top of a mass of powder can only tilt this much toward the horizontal. The funnel that was attached to a stand at a specific height was left open to let the granules flow through (h).

Once the heap of granules had formed, the width and height were measured in order to determine the angle of repose.[25]

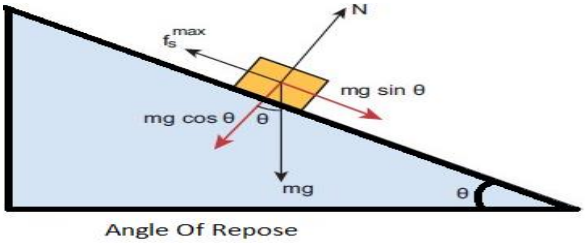

Fig 4: Angle of Repose.

7. Analysis of morphology

A scanning electron microscope was used to characterise the surface of the produced beads. To examine the sample pan's surface morphology, beads coated in gold ions are put directly on it.

8. Analysis of particle size

By using an optical microscope with a stage micrometre and calibrated eyepiece, the size of the produced beads' particles was measured, and the distribution of particle sizes was estimated.

9. Measurement of percentage yield

Beads were gathered and measured. Mass that was actually measured was split by the sum of all the materials that went into making the beads.

10. Efficacy of Drug Entrapment

For testing purposes, beads containing 100 mg of the medication equivalent were consumed. Crushed beads are extracted repeatedly with aliquots of 0.1N hydrochloric acid, the amount of drug entrapped was determined. The resulting extract was transferred to a 100-ml volumetric flask, and 100 ml of 0.1N HCl was added to get the volume up to 100 ml. After filtering the solution, the absorbance at the maximum wavelength was measured against the suitable blank.

11. In vitro buoyancy study

The surface of a USP dissolving device type II containing 900 ml of 0.1 N hydrochloric acid solution containing 0.02% Tween 80 was covered with beads (300 mg). A paddle rotating at 100 rounds per minute swirled the solution for 12 hours. The floating and settled

beads were collected, dried, and weighed individually. The buoyancy percentage was calculated by dividing the mass of the floating beads by the total mass of the beads.

12. Measurement of Moisture Content

An IR moisture balance was used to measure the amount of moisture in the beads, which were heated to 60 degrees Celsius for ten minutes.

13. Interaction between drug and an excipient

FTIR and HPLC are both used to measure it. Drug-excipient interaction is indicated by the emergence of a new height and the elimination of previous drug and excipient peaks.

Advantages Of Floating Drug Delivery System

1. Increasing the drug's bioavailability: Some medications' bioavailability, such as Levodopa, Drug delivery is greatly increased when using polymeric formulations with controlled release and gastric retention as opposed to non-gastric retention formulations.
2. First-pass hepatic biotransformation enhancement: The pre-systemic metabolism of the drug may be significantly increased when it is supplied to metabolic enzymes (cytochrome P-450, in particular CYP-3A4) in a regulated manner as opposed to by a bolus intake.
3. Continuous administration of medication.
4. Targeted medication treatment for proximal GI tract conditions: It might be useful for stomach local therapy to provide medication over an extended period of time using a floating device.[26]
5. Decreased variability of medication concentration in plasma: drug concentration variations are lessened, and undesirable effects that depend on concentration and are associated with peak levels can also be reduced.
6. Decrease in the human body's counteractivity: drugs with slow absorption into the body have less counteractive effects than those with faster absorption rates.
7. Prolonged period versus focused effort: The maintained mode of administration allows for the longer period.
8. Enhanced Selectivity of Receptor Activation: The pharmacological effects are increased by FDDS because it reduces the variance in drug concentration over the critical concentration.[27]
9. Drug delivery that is site-specific.
10. The prolonged and sustained release of medications from dosage forms that deliver local therapy in the GIT can be produced via gastroretentive drug delivery.
11. Drug systemic exposure is reduced to a minimum or eliminated thanks to the controlled, gradual release of the medication in the gastroretentive dose form, which offers appropriate local action at the sick site.
12. This drug delivery method reduces adverse drug effects by targeting a specific spot.
13. Drug concentrations and adverse effects fluctuate less with gastroretentive dosage forms. As a result, consequences that depend on concentration and are connected to maximum concentration can be avoided.

Disadvantages of Floating Drug Delivery System

1. Stomach retention is influenced by a number of variables that are never constant, such as gastric motility, pH, and the presence of food. Thus, it is impossible to forecast buoyancy.[28]
2. Drugs that irritate the stomach mucosa should not be used in the formulation of the floating medication delivery device.[28]
3. In a sleeping patient, floating tablets' stomach emptying may happen at random. As a result, the patient shouldn't take their floating pill dose right before bed.[29]
4. Drugs with problems with solubility and stability in stomach fluids should not be used to create floating drug delivery systems.[29]
5. For the preparation of the floating medication delivery system, medicines that go through the first pass metabolism should not be used.[29]
6. A strong field must exist in the stomach for the medication to float and function properly.[30]
7. Drugs that are unstable in the stomach's acidic environment should not be used to create a floating medication delivery system.[30]
8. Swallowing is difficult in individuals who are unconscious and in children.[31]

Applications for Floating Drugs Delivery Systems

1. Improvement of Bioavailability

Riboflavin CR-GRDF has a much better bioavailability when administered than non CR-GRDF polymeric formulations. The degree of medication absorption is influenced by a variety of factors, including gastrointestinal medication transport as well as absorption.

2. Sustained Drug Delivery

Oral controlled-release formulations have been associated with issues with gastric residence time in the GIT. A hydrodynamically balanced system, which has a high bulk density and can persist for a long time in the stomach.

3. Site Specific Drug Delivery Systems

For drugs that are mostly absorbed by the proximal tubule or the small intestine, these systems are very helpful. The medication is delivered to the stomach gradually and under observation, ensuring enough local therapeutic levels while minimising systemic exposure. As a result, the drug's negative impact on blood supply is reduced. Additionally, the prolonged gastrointestinal availability of a site-guided administration system may lower the need for more frequent dosage. For example, riboflavin and furosemide.[32]

4. Enhancing Absorption

Drugs with limited bioavailability from the upper gastro-intestinal tract and site-specific absorption may be compounded as FDDS to increase absorption.[33]

CONCLUSION

The Floating Drug Delivery System (FDDS) is an innovative method of drug delivery that offers advantages such as enhanced bioavailability, targeted delivery, sustained release, and reduced adverse effects. By using specific polymers and excipients, it is possible to create dosage forms that can float in the stomach for an extended period of time, allowing for controlled release of the drug. This system is especially useful for medications with narrow absorption windows, unstable in the gastrointestinal tract, and require site-specific delivery. Various methods of preparation, analysis, and applications make the FDDS a promising field for drug delivery research. However, there are also challenges and limitations associated with this system, such as the variability of gastric retention, drug incompatibility with stomach fluids, and swallowing difficulties. By overcoming these challenges and further research and development, the FDDS can be optimized for more effective drug delivery and enhanced patient outcomes.

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REFERENCES

1. Sato Y, Kawashima Y. Hirofumi takeuchi, hiromitsuyamamoto. Euro J Pharm, 2004; 57: 235–243.
2. Desai S, Bolton S. A floating controlled release drug delivery system: in vitro-in vivo evaluation. Pharm Res., 1993; 10: 1321–1325.
3. Reddy LHV, Murthy RSR. Floating Dosage Systems in Drug Delivery. Critical Reviews in Therapeutic Drug Carrier Systems, 2002; 19(6): 553–585. Available from: https://dx.doi.org/10.1615/critrevtherdrugcarriersyst.v19.i6.20.
4. Garg S, Sharma S. Gastroretentive Drug Delivery System. Business Briefing: Pharmatech, 2003; 160–166.
5. Roy HM. U.S. Patent no. 4055178, 1977.
6. Khan A. D., et al. Floating Drug Delivery System: An Overview. Int. J. PharmTech Res., 2010; 2(4): 2497-2505.
7. Sarawade A., RatnaparkhiM. P., Chaudhari S. Floating Drug Delivery System: An Overview.Int. J. Res. Dev. Pharm. L. Sci., 2014; 3(5): 1106 – 1115.
8. Vyas S. P., Khar R. K. Controlled drug delivery: Concepts and advances. Vallabh Prakashan, 2002; 1: 123-231.
9. Garg, R. and Gupta G.D., Progress in controlled gastroretentive delivery systems. Trop J Pharm Res., 2008; 7(3): 1055- 1066.
10. Nayak, A.K., Maji, R. and Das, B. Gastroretentive drug delivery systems: a review. Asian J Pharm Clin Res., 2010; 3(1): 2- 10.
11. Dave, B. S., Amin, A. F. and Patel M., Gastrorentive drug delivery system of ranitidine HCl formulation and in vitro evaluation. AAPS Pharma Sci Tech., 2004; 5: 1-10.
12. Hejazi, R. and Amiji, M., Stomach-specific anti-H. pylori therapy. I: Preparation and characterization of tetracycline of a floating multiple-unit capsule, a high-density loaded chitosan microspheres. Int J Pharm., 2002; 235: 87- 94.
13. Sawicki, W., Pharmacokinetics of verapamil and nor verapamil from controlled release floating pellets in humans. Eur J Pharm Biopharm., 2001; 53: 29-35.
14. Ojha A. Floating drug delivery system: A review. Journal of Drug Delivery and Therapeutics, 2014; 4(2): 130-4. https://doi.org/10.22270/jddt.v4i2.777.
15. Datir SK, Patil PB, Saudagar RB. Floating type drug delivery system: a review. J Drug Deliv Ther, 2019; 9(2): 428-32. https://doi.org/10.22270/jddt.v9i2.2492
16. Patil P, Baviskar P, Saudagar RB. Floating Drug Delivery System: A comprehensive review. J Drug Deliv Ther., 2019; 9(3-s): 839- 46. https://doi.org/10.22270/jddt.v9i4-s.3384
17. Chandel A, Chauhan K, Parashar B, Kumar H, Arora S. Floating drug delivery systems: A better approach. Int Curr Pharm J., 2012; 1(5): 119-27. https://doi.org/10.3329/icpj.v1i5.10283
18. Saikrishna K, Rao VUM, Kiran RS, Raju B, Keerthi LM, Dutt AG, et al. Floating Bilayer Drug Delivery Systems - A Review of Novel Approach. Pharmanest [Internet], 2014; 5(4): 2237-41. Available from: http://linkinghub.elsevier.com /retrieve/pii/S02715309140008 6X.
19. Patil P, Baviskar P, Saudagar RB. Floating Drug Delivery System: A comprehensive review. J Drug Deliv Ther., 2019; 9(3-s): 839- 46. https://doi.org/10.22270/jddt.v9i4-s.3384
20. Lende LK, Banerjee SK, Gadhave MV, Gaikwad DD, Gaykar AJ. Review on: Bilayer floating tablet. Asian Journal of Pharmaceutical Research and Development, 2013 Jan 1; 31-9.
21. Jain AK, Hatila U, A review on floating drug delivery system, International Journal of Pharmaceutical Studies and Research, 2011; 2(3): 1-6.

22. Vidyadhara S, Rao PR, Prasad JA, Development and In-Vitro Kinetic of propanolol hydrochloride controlled release matrix tablets, The Indian Pharmacist, 2006; 66-70.
23. Nandigoti J, Shayeda, Floating drug delivery system, International Journal of Pharmaceutical Sciences and Nanotechnology, 2009; 2(3): 595-604.
24. Shoufeng L, Senshang L, Chein YW, Daggy BP, Mirchandani HL, Statistical optimization of gastric floating system for oral controlled delivery of calcium, AAPS Pharm Sci Tech, 2001; 2: 1-12.
25. Sharma N, Agarwal D, Gupta MK, Khinchi MP, A comprehensive review on floating drug delivery system, International Journal of Research in Pharmaceutical and Biomedical Sciences, 2011; 2(2): 428-441.
26. Kaur B, Sharma S, Sharma G, Saini R, Singh S, Nagpal M, Jain UK, Sharma M. A Review of Floating Drug Delivery System. Asian Journal of Biomedical and Pharmaceutical Sciences, 2013; 3(24): 1- 6.
27. Chikhalikar SS and Wakade RB: Floating Drug Delivery System – An Approach To Oral Controlled Drug Delivery. International Journal of PharmTech Research, 2012; 4(4): 1812-26.
28. Parmar PD, Pande S, Shah SH, Sonara N, Patel GH. Floating drug delivery system: A novel approach to prolong gastric retention. World J Pharmacy Pharm Sci., 2014 Feb 25; 3(4): 418-44.
29. Karudumpala S, Chetty M, Gnanaprakash K, Venkatesh B, Sankar P. A review on bilayer floating tablets. Int J Res pharm Sci., 2013; 4(2).
30. Roshani K, Panda P, Vishwakarma DK, Verma NK. A brief review on bilayer floating A brief review on bilayer floating tablet. International Journal of Advances in Pharmaceutics, 2017; 6(3): 70-78.
31. Sharma N, Kakkar S. Floating Tablet: a Review. Int J Recent Adv Sci Technol, 2015; 2(4): 1-8. https://doi.org/10.30750/ijrast.241
32. Farooq SM, Sunaina S, Rao M, Venkatesh P, Hepcykalarani D, Preama R. Floating Drug Delivery Systems: An updated Review. Asian Journal of Pharmaceutical Research, 2020 Mar 9; 10(1): 39-47. https://doi.org/10.5958/2231- 5691.2020.00009.X
33. Patial K, Dua JS, Menra M, Prasad DN. A Review: Floating Drug Delivery System (FDDS). Pharmaceutical Research World Journal Of Pharmaceutical Research, 2016 Mar 29; 5(6): 614-33.