

A NOVEL APPROACH: FLOATING DRUG DELIVERY SYSTEM.

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ABSTRACT

The Gastroretentive drug delivery system (GRDDS) is the novel approach of retaining dosage form in stomach after oral administration and to ensure release of the drug in a controlled and prolonged manner, to its absorption sites in gastric region. The drug which shows characteristic property in acidic media or upper part of gastrointestinal tract mainly in the gastric region, are most suitable candidate for such gastro retentive dosage form. The drugs which have short half-life can remain for several hours and gives prolong gastric residence time of drugs and significantly enhances absorption. Mechanism behind the principle of floating is density, bulk density in floating drug delivery system (FDDS) is more than the gastric fluids and therefore, they remain buoyant or float in the stomach for a prolong period without disturbing gastric emptying rate. and resulting into increased in gastric residence time and a good control of plasma drug concentration. The main purpose of this paper is to review the concept of gastroretentive drug delivery systems with the recent literature and advanced technology used in the development of this system.

Key words: Novel drug delivery, floating drug delivery system, polymers for FDDS, Marketed formulations.

1. Drug delivery

Drug delivery refers to novel method of formulations, manufacturing techniques, storage systems, and technologies involved in transportation of a pharmaceutical compound to its active target site to achieve a desired pharmacological and therapeutic effect.[1]

1.1 Drug delivery system: Drug delivery system: A drug delivery system (DDS) is defined as a formulation or a device that allow a therapeutic substance to selectively reach its site of action and thereby increase its potency and efficacy. If drug reaches to the nontargeted cells, organs, or tissues it will produces the adverse effect generally known as unwanted effects or adverse effect or side effects. Drug delivery has the potentiality to have a tremendous impact on treatment of retinal diseases. Most of the drugs that are effective to treat retinal conditions, but some of those drugs have limitation of delivery issues like molecules must have to cross the blood-eye barrier, be reside for long time, or should have minimum or no side-effects. [1,2]

The challenges to deliver the drug with minimum concentration at site of action for extended periods or in a localized delivery system that can be solved with drug delivery technology, whether it can be solved by using cellular delivery systems, microelectromechanical (MEMs)-based devices, polymer matrices, or gene delivery systems. The method through which a drug is delivered can have a significant effect on its efficacy. Most of drugs have an optimum concentration range generally known as therapeutic range within which maximum therapeutic action is obtained, and concentrations above or below this range can be toxic or produce no therapeutic effect at all. Although, the very slow progress in the efficacy of the treatment of severe diseases, has suggested that there is need of a multidisciplinary approach to the deliver the therapeutics to targeted tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated. These new strategies, usually called drug delivery systems (DDS), which are based on interdisciplinary approaches that combines polymer science, pharmaceuticals, bioconjugate chemistry, and molecular biology.^{2,3,4} To reduce drug degradation and drug loss, to prevent unwanted or harmful side-effects and to enhance drug bioavailability and the fraction of the drug accumulated in the targeted area, various drug delivery and drug targeting systems are currently under development. Controlled and Novel Drug Delivery which was only a dream or at best a possibility is now a reality. [2,3]

During last decade many pharmaceutical companies and other scientists have carried out comprehensive investigations in this field of drug research. The substances that carry the drug to the targeted site are called as drug carriers and are soluble polymers, microparticles made of insoluble or biodegradable, natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes, and micelles. The carriers must be slowly biodegradable, stimuli-reactive (e.g., pH- or temperature-sensitive), and even targeted (e.g., by conjugating them with specific antibodies against certain characteristic components of the area of interest). Targeting is the ability to administer the drug-loaded system to the site of action. Major mechanisms can be distinguished for addressing the desired sites for drug release:

1. **Passive targeting**
 - a) Leaky vasculature
 - b) Direct local application
2. **Active targeting**
 - a) Carbohydrate targeted
 - b) Receptor targeted
 - c) Anti-body targeted

An example of passive targeting is the preferential accumulation of chemotherapeutic agents in solid tumors as a result of the increase vascular permeability of tumor tissues compared with healthy tissue. A key strategy that allows active targeting involves the surface functionalization of drug carriers with ligands that are selectively recognized by receptors on the surface of the cells of targeted site.[5] Since ligand-receptor interactions can be extremely selective, this could allow a more specific targeting of the site of interest. Any drug delivery system may be defined as a system consisting of:

- ✓ Drug formulation
- ✓ Medical device or dosage form/technology to carry the drug inside the body
- ✓ Mechanism for the release. [5]

IMPORTANCE OF DDS:

1. Selectively delivers drugs to the site of action.
2. Enhance stability of drug molecules.
3. It overcome biological barriers for drug transportation.
4. Target drugs via active or passive mechanism.
5. Drug delivery system controls pharmacokinetic profile of drug molecule.
6. It enhances solubility of drug molecule. [4,5]

2. NOVEL DRUG DELIVERY SYSTEM: Conventional drug delivery includes the formulation of the drug into a suitable form, such as a compressed tablet for oral administration or a solution for intravenous administration. These dosage forms had serious limitations which includes higher dosage required, lower effectiveness, toxicity and adverse side effects. New drug delivery systems have been developed or are being developed to encounter the limitation of the conventional drug delivery systems to meet the need of the healthcare profession.[6]

This system can be characterized as controlled drug release system and targeted drug delivery system. Ndds is an advanced drug delivery system which improves drug potency, control drug release to provide sustained therapeutic effect, greater safety, and target a drug specifically to a desired tissue or organ. In another words NDDS refers to the approaches, formulations, technology and systems for transporting a pharmaceutically active compound in body as needed to safely attain its desired therapeutic effects.[7]

The therapeutic benefits of these new systems include:[1]

- ✓ Increased efficacy of the drug
- ✓ Site specific delivery
- ✓ Decreased toxicity/side effects
- ✓ Increased convenience
- ✓ Viable treatments for previously incurable diseases

- ✓ Potential for prophylactic applications
- ✓ Better patient compliance.

There is no uniform and established definition of drug delivery systems. It is assumed that the drug delivery system should be based on two basic or distinct parameters: Route of entry/route of administration (A) and Dosage form (B). Any member of the cartesian product of (A X B) is defined as a drug delivery system. Such a definition implies that there are a vast number of members in this group. Many of them may not even be feasible, while many others may not be relevant. So, the set of most relevant new drug delivery systems is that include use of carriers to deliver drug to the site of action is as follows: Carrier based drug delivery system:[5]

1. Liposomes
2. Nanoparticles
3. Microspheres
4. Monoclonal antibody.
5. Niosomes
6. Ethosomes
7. Resealed erythrocytes.

3. FLOATING DRUG DELIVERY SYSTEM:

Floating drug delivery systems (FDDS) are invented to retain the drug in the stomach mainly in upper part of GIT and applicable for drugs with poor solubility and low stability in intestinal fluids. The basis behind FDDS is making the dosage form of less density than the gastric fluids to float on them. FDDS are hydro-dynamically controlled low-density systems having sufficient buoyancy to float over the gastric contents (juices or secretions) and remain buoyant in stomach without affecting the gastric emptying rate for a prolonged period of time and release drug continuously. The residual system is emptied from the stomach with the release of the drug. This increases gastric residence time and good control over plasma drug concentration fluctuation.[7]

The principle of buoyant preparation provides a simple and practical proposal to obtain increased gastric residence time for the dosage form and sustained drug release. Prolongation of gastric retention of a delivery system is desirable for achieving the greater therapeutic efficacy of the drug substance under certain conditions. For example, drugs which show better absorption at the proximal part of the gastrointestinal tract and drugs having low solubility and get degraded in alkaline pH of intestine found efficient in prolonging gastric retention.[8]

In addition, for sustained drug delivery to the stomach and proximal small intestine to treat certain ulcerative conditions which includes crohn's disease, prolonging gastric retention of therapeutic moiety and hence provide numerous advantages including enhance bioavailability and therapeutic efficacy with reduction of dose or dosing frequency.[9]

Classification of FDDS with consideration of its physiochemical behaviour and appearance are as follows: Classification of floating drug delivery system:

3.1 Classification of floating drug delivery system:

1. **Effervescent system**
 - a. **Gas generating system**
 - i. **Floating tablets**
 - ii. **Floating pills**
 - b. **Volatile liquid system:**
 - i. **Intragastric osmotically controlled**
 - ii. **Gastrointestinal inflatable**
2. **Non-effervescent system:**
 - I. **Hydrodynamically balanced system**
 - II. **Matrix layered tablet**
 - III. **Alginate beads**
 - IV. **Hollow microsphere/ microballoons**
3. **Raft forming system**

Floating drug delivery system (FDDS) is a significant approach for prolongation gastric retention time. Floating drug delivery system not only prolongs GI residence time but also enhances bioavailability, reduces drug waste and improves solubility of drugs that are less soluble or insoluble in high pH environment. The prolongation of

gastric retention is essential to achieve the control over gastric retention time so it helps to maintain the controlled release system in the GIT for a longer period of time.[9]

Several approaches are presently used in the prolongation of the gastric residence times (GRT) including:

- ✓ floating drug delivery systems (FDDS),
- ✓ Low density systems,
- ✓ Raft systems incorporating alginate gels,
- ✓ Bio adhesive or Mucoadhesive systems,
- ✓ High-density systems,
- ✓ Super porous hydrogels
- ✓ magnetic systems.

Floating systems or Hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents of stomach and remain buoyant in the stomach without affecting the gastric emptying rate for a prolong period of time.[12] This results in prolonging gastric retention time and a greater control of the fluctuations in plasma drug concentration.

3.2 Advantages of FDDS: Floating dosage systems are delivery systems with gastric retentive behaviour and offer several advantages in drug delivery.

Some of these include:[10]

Increase Bioavailability: The bio-availability of some drugs (e.g. riboflavin and levodopa) CR-GRDF is significantly increased in comparison to administration of NON-GRDF Control release polymeric formulations.

Enhanced First-Pass Metabolism: When the drug is exposed to the metabolic enzymes (cytochrome P-450, in particular CYP-3A4) in a sustained manner, the pre-systemic metabolism of the tested compound may be considerably enhanced rather than by a bolus input.

Decrease frequency of Dosing: The drugs having short biological half-life, an sustained drug release is advantageous and reduce dose and frequency of drug.

Increase patient compliance: slow input from FDDS may result in a flip-flop pharmacokinetics and it decrease the dose frequency. This feature is an associated with improved patient compliance and thus improves the therapy.

Targeted therapy for upper GIT: The prolonged and sustained administration of the drug using FDDS approach to the stomach may be useful for local therapy in the stomach

Decrease fluctuations in plasma Drug concentration: The fluctuations in plasma drug concentration is reduced, and concentration-dependent adverse effects that are related with peak concentrations can be prevented. This feature is essential for drugs having a narrow therapeutic index that makes it possible to obtain selectivity in the elicited pharmacological effect of drugs that activate different types of receptors at different concentrations.

Reduced counter-activity of the Body: Slow and sustained release of the drug into the body reduces the counter activity leading to higher drug efficiency.

Extended time over effective concentration: The sustained mode of administration enables extension of the time which allows to release total amount of drug present in drug formulation.

Enhanced Receptor activation selectivity: FDDS minimizes the plasma-drug concentration fluctuation over a critical (Effective) concentration and thus increases the pharmacological effects and improves the clinical outcomes.

Reduced adverse effect at the Colon: Retention of the drug in GRDF at stomach decreases the amount of drugs that reaches the colon and thus prevents drug degradation in the colon.

Site specific Drug Delivery: A floating dosage form is a widely accepted approach for the drugs which have very limited absorption sites in upper part of GIT.

3.3 Selection criteria for floating drug delivery system: [10]

The Floating systems are for drugs having local action in the Stomach e.g. Antacids. Drugs with low pKa, that does exhibit unionized characters.

Acidic substances like aspirin cause irritation on the stomach wall when come in contact with it. Hence FDDS is useful for the administration of aspirin and other similar drugs.

The Floating systems is suitable for drugs absorbed through the stomach. e.g. Ferrous salts, antacids.

FDDS provides some advantages like the delivery of drugs with narrow absorption windows in the small intestinal region.

Certain types of drugs having benefit from using FDDS. These include:

Drugs acting **locally in the stomach**. Eg: misoprostol

Drugs having **short half-life** eg: captopril

Drugs that are **primarily absorbed in the stomach**. Eg: amoxycillin

Drugs that are **poorly soluble at an alkaline pH**. Eg: diazepam verapamil etc

Drugs which have a **narrow window of absorption**.

Drugs **absorbed rapidly from the GI tract**. Eg: tetracycline metronidazole etc.

Drugs that **degraded in the colon**.eg: ranitidine, metformin etc.

The drug which is **required in small dose**.

3.4 Disadvantages /limitation of floating drug delivery system:

Requires a high level of fluids in the stomach: The major disadvantage of floating system is requiring a high level of fluids in stomach for drug delivery to float and work efficiently.

Drugs having solubility and stability problems: These systems are not applicable for those drugs that have solubility or stability problem in the GI tract.

Drugs that well absorbed from GIT: Drugs like Nifedipine, Propranolol etc. which are well absorbed throughout GIT and which undergoes first pass metabolism are not be desirable candidate.

Drugs that causes irritation to gastric mucosa: Drugs (like NSAIDS) that can cause irritation and lesions to gastric mucosa are not feasible to be formulated as floating drug delivery systems.

Drug that degrades in acidic pH: The drug candidates that are unstable in the stomach acidic environment are not suitable for FDDS systems.

Nature of dosage form: Ability to float depend in the hydration state of dosage form and Dosage form needs faster swelling properties as well as complete swelling of the system. It must be achieved before the gastric emptying time.

Gastric secretion's: The mucus from secretory cells present on the walls of the stomach is in a state of continuous renewal which results in unpredictable adherence.

Requires large amount of water: The dosage form should be administered with full glass of water (200-250 ml).

These systems do not shows significant advantages over the conventional dosage forms for drugs which get absorbed throughout gastrointestinal tract.

3.5 Factors Affecting Floating Drug Delivery System:

1. Density of dosage form

Floating is function of dosage form buoyancy that depends on density. Density of dosage form should be less than the gastric secretions (contents) (1.004gm/ml). A density of less than 1.0 gm/cm³ is required to show floating property. Hence dosage forms which have density lower than the gastric contents are able float to on surface while high density systems sink to bottom of the stomach.

2. Shape and size of dosage form

The shape and size of the dosage form are factors that alters gastric retention. Dosage form having a diameter of more than 7.5 mm are reported to increase GRT as compared to those which have diameter of 9.9 mm. The dosage form having tetrahedron shape and ring shape devices with flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to exhibit better GIT for 90 to 100 % retention at 24 hours compared with other shapes.

3. Food intake and its Nature

Food intake, viscosity and volume of food, caloric value and frequency of feeding shows a greater influence on the gastric retention of dosage forms. The presence or absence of food in gastrointestinal tract (GIT) affects the gastric retention time (GRT) of the dosage form. Indigestible polymers or fatty acid salts may alter the motility pattern of the stomach to a fed state hence leads to decreased gastric emptying rate and prolonging drug release.

4. Caloric content

The gastric retention time (GRT) may be increased by 4 to 10 hours if taken with meal having high in proteins and fats. Floating can increase by over 400 minutes when successive meals are given as compared with a single meal due to the low frequency of migrating myoelectric complexes (MMC).

5. Effect of gender, posture and age

Females generally have slower gastric emptying rates than male. The effect of posture does not have much more difference in the mean gastric retention time (GRT). In case of elderly persons, especially those over 70, have a significantly longer GRT so gastric emptying is usually slowed down. Disease condition like diabetes and crohn's disease etc also affect drug delivery.

6. Fed or Unfed State

During fasting state the gastric motility is described by periods of strong motor activity or the migrating myoelectric complexes (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and if timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However in fed state, MMC is delayed and GRT is considerably longer as compared to fasting state.

7. Concomitant drug administration

Anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramide and cisapride can alters floating time.

3.6 Polymers used in floating delivery:

A polymer is a large molecule, or macromolecule, composed of many repeated subunits form to produce polymer. Because of their broad range of properties, both synthetic and natural polymers play an essential role in everyday life.

Polymers are of generally of two types natural polymers and synthetic polymers. Both have different advantages; some combinations have good advantages and serve excellent floating property and are enlisted below:

Sr no	Polymer / ingredient	Characteristic
1	EudragitS100 Eudragit	A good floating behaviour was observed, whereas the dissolution rate is very slow, because the solubility of Eudragit at acidic pH of stomach is very low.
2	HPMC	1. prolong gastric residence time and increased bioavailability 2. Sustained release floating effect as well as good swelling index 3. More sustained release of drug with high buoyancies.
3	HPMC-Guar gum	Floating lag time extends with an increase in swelling behaviour.
4	HPMC-Locust bean gum	Follows zero order kinetics with enhance the gastric residence time
5	Polyacrylate, HPMC and chitosan gel	Sustained drug release with increased swelling behaviour of dosage form
6	EC and HPMC	Increased gastric residence time with a reduction in dose of drug, amount of drug, and dosing interval
7	Polyvinyl acetate	Follows zero order kinetics profile and decrease gastric emptying time.

3.7 Evaluation of Floating Dosage Forms

Pre-compression parameters:

a) Angle of Repose (Θ)

The presence of frictional forces in a loose powders or granules can be identified and measured by angle of repose.

angle of repose is the maximum angle possible between the horizontal plane and the surface of a pile of powder or granules. The powders are allowed to flow through the funnel fixed to a stand at definite height (h). measure the height and radius of the heap of granules /powders to calculate angle of repose.

$$\tan \Theta = h/r$$

$$\Theta = \tan^{-1} (h/r)$$

Where,

Θ = angle of repose

h = height of the heap

r = radius of the heap

b) Compressibility Index

The flowing ability of powder can be measured by comparing the bulk density (ρ_0) of powder and tapped density (ρ_t) of powder and the rate at which it packed down. Compressibility index was calculated by –

Compressibility index (%) = $\rho_t - \rho_o \times 100 / \rho_t$

Where,

ρ_o = Bulk density g/ml

ρ_t = Tapped density g/ml.

II. Post-compression parameters:

1. Size and Shape Evaluation

Particle size plays an important role in determining the rate of solubility and bioavailability of active pharmaceutical ingredient. The particle size of the formulation can be determined using Sieve analysis, Air elutriation analysis, Photo analysis, Optical microscope, Electro resistance counting methods (Coulter counter), Sedimentation techniques, Laser diffraction methods, ultrasound attenuation spectroscopy.

2. Tablet Dimensions

Thickness and diameter of floating tablets were measured using a calibrated vernier caliper. Picked randomly three tablets of each formulation and measure the thickness of individual tablets.

3. **Hardness:** The ability of a tablet to withstand mechanical shocks while Handling and transportation is called as hardness. The hardness of the tablets was measured by using Monsanto hardness tester, erweka hardness tester etc. unit of hardness can be expressed in kg/cm². Picked Three tablets randomly and hardness of the tablets was determined.

4. Friability test

The friability of tablets can be determined by using Roche Friabilator. It was expressed in percentage (%). Ten tablets were initially weighed (W initial) and transferred into friabilator. The friabilator must operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (Wfinal). The % friability was then calculated by :

$$\%F = 100 (1 - W_0/W)$$

Limit: % Friability of tablets less than 1% was considered and acceptable.

5. **Tablet density** is one of an important parameter for floating tablets. The tablet would float only when the density of tablet is less than that of gastric fluid (1.004). The density was determined using following relationship.

$$V = \pi r^2 h$$

$$d = m/v$$

v = volume of tablet (cc)

r = radius of tablet (cm)

h = crown thickness of tablet (g/cc)

m = mass of tablet

6. Weight Variation Test

From each batch ten tablets were selected randomly and weighed individually to check for weight variation. Compare this weight variation according to Pharmacopoeial standards.

7. Buoyancy / Floating Test

The time taken by tablet to its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to float on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant or float is called Total Floating Time (TFT).

8. Swelling Study

The swelling behaviour of a dosage form was measured by studying its weight gain or water uptake. Swelling studies are performed in order to calculate molecular weight of swollen polymers. The dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake was measured in terms of percent weight gain, as given by the equation.

$$\text{Swelling ratio} = \text{Weight of wet formulation} / \text{Weight of formulations}$$

3. Surface Topography

The surface topography and structures can be determined using scanning electron microscope(SEM) which is operated with an acceleration voltage of 10k.v, Contact angle meter, Atomic force microscopy (AFM) and Contact profilometer.

4. Determination of Moisture Content

Karl fisher titration is best suited for For the determination of moisture content of the prepared formulations. The other methods used are Thermo gravimetric methods, Vacuum drying, Air oven method, Freeze drying, and Moisture Meters.

6. Determination of the Drug Content

Percentage drug content of prepared formulation indicates amount of drug present in formulations. It should not exceed the limits mentioned in the standard monographs. The drug content can be determined by using Near infrared spectroscopy (NIRS), Micro titrimetric methods, HPLC, HPTLC methods, Inductively Coupled Plasma

Atomic Emission Spectrometer (ICPAES) and also by using spectroscopy techniques as per standard monographs.

7. Percentage Entrapment Efficiency

The three methods used to determine entrapment efficiency include pressure Ultra filtration, Ultra-centrifugation, and Micro dialysis method. Percentage entrapment efficiency is responsible for quantifying the phase distribution of drug in the prepared formulations.

8. In-vitro Release Studies

In vitro release studies (USP dissolution apparatus (usp-24)) are performed to determine the amount of the drug that is released at a definite time period from each formulation. Franz diffusion cell system and synthetic membrane are used for liquid formulations whereas different types of dissolution apparatus are used to perform drug release studies of solid preparation.

9. Powder X-ray Diffraction

For the study of poly-crystalline materials powder x-ray diffraction is the predominant tool. Irradiation of samples are done with α -radiation and analyzed between 2 θ C and 60 θ C. The 30KV and 30mA voltage and current used respectively (30).

10. Fourier Transforms Infrared Analysis

Fourier transform infrared spectroscopy (FT-IR, Shimadzu, and Model-RT-IR-8300) is a technique is mostly used for identifying organic, inorganic materials, polymeric materials and most precisely functional group determination. The pellets are prepared by using KBr-press under hydraulic pressure of 150kg/cm² and then the spectra scanned over the wave number range of 3600 to 400 cm⁻¹ at the ambient temperature.

11. Differential Scanning Calorimetry (DSC)

DSC is generally used to determine water of hydration of pharmaceuticals preparations. Thermo grams of formulated preparations are obtained by using DSC instrument which is equipped with an intercooler. To calibrate the DSC temperature and enthalpy scale Indium/Zinc standards are used. Sample preparations are hermitically sealed in an aluminium pan and then heated at a constant rate of 10°C/min; over a temperature range of 25° C – 65°C. Nitrogen gas is purged at the flow rate of 50ml/min to maintain inert atmosphere.

3.8 Marketed formulations:

Sr.no	Brand name	Drug dose	Dosage form
1.	Val release	Diazepam (15 mg)	Floating Capsule
2.	Topalkan	Al-Mg Antacid	Floating liquid alginate preparation
3.	Convion	Ferrous sulphate	Colloidal gel forming FDDS
4.	Cytotech	Misoprostol (100 μ g/200 μ g)	Bilayer floating Capsule
5.	Cifran OD	Ciprofloxacin (1 gm)	Gas generating floating form
6.	Liquid Gaviscon	Al hydroxide (95mg), Mg Carbonate (358mg)	Effervescent floating liquid alginate preparation
7.	Madopar HBS	Levodopa & Benserazide	Floating CR capsule
8.	Prolopa	Levodopa, benserazide	Floating capsule
9.	Oflin Od	Ofloxacin	floating tablets
10.	Almagate Flatcoat	Aluminium-Magnesium Antacid	Floating dosage form

3.9 CONCLUSION

Drug delivery using various floating drug delivery system (FDDS) approaches has emerged as an effective means for controlled drug delivery and also enhancing the bioavailability of many drug candidates. Controlled release floating drug delivery system is a promising delivery system which provides a potential approach for gastric retention. Developing an effective FDDS is challenging and the drug delivery system must remain for sufficient time in stomach. FDDS has an additional advantage for the drugs that are absorbed in the upper part of the gastrointestinal tract mainly in stomach and which shoes drug release in acidic media. Many drugs have been prepared as floating drug delivery systems to attain sustained release and restricting the drug to release in stomach. The most important criteria which has to be observed for the productions of a floating drug delivery system is that the prepared dosage form always have density less than that of gastric fluid. Thus, it can be concluded that floating dosage forms serve as best in the treatment of GIT diseases and for prolonging action of

drugs with a short half-life and eliminate problem arises during formulation such as low bioavailability and extensive first pass metabolism.

4.REFERENCES:

- [1] Bhagwat RR et al, novel drug delivery system an overview. *International journal of pharmaceutical sciences and research* 2013;4(3);970-982.
- [2] Reddy P.D. et al, Recent advances in novel drug delivery systems. *IJPTR*,2010; 2(3); 2025-2027.
- [3] Manivannan R.et al, Recent advances in novel drug delivery system. *IJRAP*.2010; 1(2); 316-326.
- [4] Beena Kumari, Recent Development in Floating Drug Delivery System: A Review. *Asian Journal of Pharmacy and Pharmacology* 2018; 4(2): 131-139.
- [5] Kirti Patial Et Al, A Review: Floating Drug Delivery System (Fdds), *Earthjournals* Volume 4, Issue 3, 2015.
- [6] P.G.Yeole et al, Floating drug delivery need and development, *Indian journal of pharmaceutical sciences*; 2005, 67(3):265-272.
- [7] Kumar Mukesh et al, floating drug delivery system: a innovative approach, *journal of drug delivery & therapeutics*; 2012, 2(6), 117-123.
- [8] Mirmeeera Girish Niharika Et Al, Overview On Floating Drug Delivery System, *International Journal Of Applied Pharmaceutics*; Vol 10, Issue 6, 2018.
- [9] Dubey J and Verma N: Floating Drug Delivery System: A Review. *Int J Pharm Sci Res* 2013; 4(8); 2893-2899. doi: 10.13040/IJPSR.0975-8232.4(8).2893-99.
- [10] Ziyaur R, Mushir A and Khar RK. "Design and Evaluation of bilayerfloating tablets of captopril", *Actapharmaceutica*, 2006;5(6):4957.
- [11] Sharma N. Et Al, Floating Tablet: A Review, *International Journal Of Recent Advances In Science And Technology*, 2015; 2(4): 1-8.
- [12] Hetal N and Kikani A. , "Thesis on, Floating Drug Delivery System" *The North Gujarat University, Patan*. 2001; 11-12.
- [13] Christian, Vishal, T. Ghedia, and V. Gajjar. "A review on floating drug delivery system as a part of GRDDS." *IJPRD* ,2011,3(6): 233-241.
- [14] Kandwal m.et al, floating drug delivery system: a novel approach, *the pharma innovation – journal*; vol. 3 no. 3. 2014.
- [15] Narang N. An Updated Review On: Floating Drug Delivery System (FDDS). *Int J App Pharm* 2011; 3(1):17.
- [16] Chandel et al,Floating drug delivery systems: A better approach, *International Current Pharmaceutical Journal* 2012, 1(5): 110-118.
- [17] Kadivar A,et al. Formulation and In Vitro, In Vivo Evaluation of Effervescent Floating Sustained-Release Imatinib Mesylate Tablet. *PLoS ONE* 10(6) (2015).
- [18] Ref: Erin B. Lavik, Baruch D. Kuppermann, Mark S. Humayun, "retina" (fifth edition)2013.