IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Review: Gastro-Retentive Bilayer Floating Tablets

Name: ABHISHEK KESHAVRAO KHILLARI (B.PHARM)

Guided By: DR. A. A. HARSULKAR (M.PHARM, PH.D)

Department: INDUSTRIAL PHARMACY M.PHARM, SGBAU UNIVERSITY,

AMRAVATI, MAHRASHTRA, INDIA.

College Name: SUDHAKARRAO NAIK INSTITUTE OF PHARMACY, PUSAD.

ABSTRACT:

The oral route is considered to most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance, and cost-effective production process. Many technological developments have resulted in the creation of controlled drug delivery systems, which have the potential to transform medication distribution and offer a multitude of therapeutic advantages. These systems address the shortcomings of conventional drug delivery methods. among the most popular methods for gastro-retentive drugs delivery. Several approaches are currently being used to prolong the GRT, including gastr-retentive drug delivery systems (GRDDS), also known as hydrodynamically balanced systems (HBS), swelling and expanding systems, high-density systems, and other delayed gastric emptying devices. One dosage form that is showing promise is floating dosage forms. By combining the right ingredients and a gas-generating agent, floating dosage forms can be made into tablets or capsules. This review on gastro-retentive drug delivery systems (GRDDS) was written with the intention of gathering the most recent research, paying particular attention to the main mechanism of floatation to accomplish gastric retention.

The current study aims to improve bioavailability by extending the gastrointestinal residence duration by the creation of a gastro retentive floating bilayered tablet. A simple UV spectro photometric method has been employed for the estimation of API at 238 nm with a Beer's range of 0-10µg/ml. Fourier transform Infrared spectroscopy confirmed the absence of any drug/polymer's interactions.

KEYWORDS: Gastro-Retentive drug delivery, Floating drug delivery, Gastric Retention Time, etc.

INTRODUCTION:

Pharmaceutical drug items are referred to as dosage forms when they are marketed in a specified format, at a specific dose, and with a particular combination of active and inactive substances. Based on their intended functions, application place, administration method, and physical state, the dosage forms can be categorized. Because it is the easiest to administer, patient compliance is high, there are less sterility concerns, and dosage forms may be designed in a variety of ways, oral administration is the most practical and preferred method of delivering drugs into the systemic circulation.

Solid oral dosage forms are most favoured over other route of drug administration due to ease of drug administration, better patient compliance and flexibility and still the most extensively used formulation, almost 90% of the formulation produced today are consumed orally. It proves that this kind of formulation is the most commonly accepted worldwide, and this is the main topic of interest for the researcher.

Gastro-Retentive Drug Delivery System (GRDDS):

Gastro- Retentive Drug Delivery Systems are meant to be retained in the stomach for a prolonged period. Thus, they provide sustained and prolonged drug release to the upper part of the gastrointestinal (GI) tract. Certain types of drugs have benefited by using gastric retentive devices. These include;

1. Acting locally in the stomach.
2. Primarily absorbed in the stomach.
3. Poorly soluble at an alkaline pH.
4. Narrow window of absorption.
5. Absorbed rapidly from the GI tract.
6. Degrade in the colon.

For the long-term treatment of many diseases, the oral route has been the primary medication delivery method. Creating an ideal bilayer tablet was the goal of the current project. It is commonly recognized that this floating dose form is a hydrodynamically balanced system (HBS). It has been suggested for the following instances that an active material should be formulated in the form of an HBS to enhance bioavailability:

(i) Having an issue with stability or dissolution in the fluids of the small intestine.
(ii) Being locally effective in the stomach.
(iii) Being absorbed only in the stomach and/or upper part of the intestine.

The stomach is divided into 3 anatomic regions: 1) Fundus, 2) Body, and 3) Antrum (pylorus). The pylorus is the valve that divides the stomach from the duodenum. The part made of fundus and body acts as a reservoir for undigested material, while the antrum is the primary location for mixing motions and propelling efforts to empty the stomach. Both when feeding and when fasting, gastric emptying takes place. Nonetheless, the motility patterns for the two states differ.

Every 2 to 3 hours, an interdigestive sequence of electrical events occurs in the stomach and intestine during the fasting state. The Migrating Myloelectric Cycle (MMC), also known as the interdigestive myloelectric cycle, is further divided into the following 4 phases.

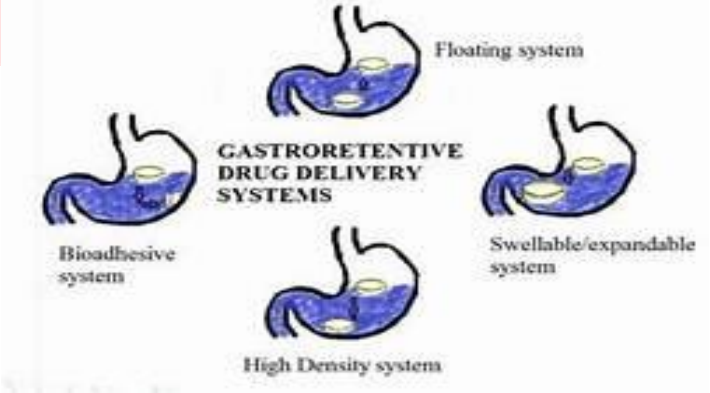

Fig.01: GRDDS

Phase I: (Basal Phase): There are rare contractions throughout this 40 to 60 min phase.
Phase II: (Pre-burst Phase): Action potentials and contractions occur sporadically throughout this 40 to 60 min phase. Both the intensity and frequency progressively rise as the phase goes on.
Phase III: (Burst Phase): sometimes known as the "Burst Phase," lasts 4 to 6 min. It consists of brief, powerful contractions that occur frequently. All of the undigested material is carried out of the stomach and into the small intestine by this wave. Another name for it is the housekeeper wave.

Phase IV: This phase, which comes in between phases III and I of 2 consecutive cycles, lasts from 0 to 5 minutes. Following consumption of a mixed meal, the contraction pattern transitions from a fed state to a fast state. Similar to phase II of the fasting state, this is also referred to as the digestive motility pattern and entails constant contractions. Food particles are pushed into the pylorus in a suspension form as a result of these contractions, which reduce their size (to less than 1 mm). The delayed commencement of the fed state in MMC causes a slowing in the rate of stomach emptying.

Classification of Gastro-retentive Drug Delivery System:

A. Low-density systems (Floating systems)

a) Effervescent system

1) Volatile liquid-containing system 2) Gas generating system 3) Matrix tablets

b) Non effervescent system

1. Colloidal gel barrier system/Hydrodynamically balance system

2. Layered Tablets: a) Single-layer tablets b) Bilayer tablets

3. Alginate beds

4. Hollow microspheres

B. High-density systems

C. Bio-adhesive or Mucoadhesive systems

D. Swelling and Expanding Systems

E. Magnetic system

F. Raft-forming systems

G. Super porous hydrogel system

H. Modified shape system

Floating Drug Delivery System (FDDS):

The floating drug delivery system (FDDS) is also called a hydrodynamically balanced system (HBS). on FDDS, the drug delivery systems float on gastric juice to prevent drug leakage from the stomach. It efficiently lengthens the release duration, increasing medication absorption. Additionally, there is less variation in the medication concentrations in blood. Diseases of the stomach and duodenum may be treated using floating drug delivery. FDDS carriers need to have a lower density than chymus and gastric juice. Therefore, medicines float and are slowly released in the stomach, compared with the convectional drug delivery methods. Most antibacterial agents have low minimum inhibitory concentration (MIC) to Helico-bacter Pylori in vitro, but are not very effective for the eradication of infection caused by Helicobacter Pylori in vivo. The main problem is the short residence time. Better stability and prolonged residence time allow more effective antibiotic penetration through the gastric mucus layer to suppress or eradicate Helicobacter Pylori in stomach, which would be achieved by FDDS.

The majority of FDDS do not float for 2–8 hours at the moment; nevertheless, the drug's float and release times must be extended. Control of the drug carrier materials has been extensively studied in earlier research investigations to achieve improved medication float and release times. created hollow spheres for FDDS with the use of the diffusion method of emulsion and solvent. The focused of these works was to use solvent diffusion to adjust the carrier density. Specifically, carrier floating behaviours are determined by solvent diffusion rates that are dominated by polymer porosity.

BILAYER TABLET:

Pharmacological therapies either require or benefit from the administration of drugs in a sequential manner. These combination formulations operate on a single dosage form, simplifying therapy and lowering or eliminating the possibility of incorrect dosing. Bilayer formulations transport multiple drugs at separate rates of administration (immediate, timed, or sustained), delivering each one individual of many another and without any pharmacokinetic or dynamic interactions. A better and more useful technology to address the shortcomings of the single-layered tablet is the bilayer tablet. Usually, conventional dosage form produces wide ranging fluctuation in drug concentration in the blood stream and tissues with consequent undesirable toxicity and poor efficiency. The idea of regulated medication delivery systems was inspired by factors including repetitive dosage and unpredictable absorption. Increasing the effectiveness of the medication by localizing it at the site of action, lowering the dosage needed, or ensuring consistent drug delivery are the main objectives of developing sustained or controlled delivery systems. Ensuring patient compliance and enhancing therapeutic efficacy and safety are the main goals of sustained release drug delivery. Bilayer tablets can be used to separate two substances that are incompatible, release two medications sequentially in combination, or create sustained release tablets, where the first layer is the initial dose that is released immediately and the second layer is the maintenance dose.

Need of Bilayer Tablets:

- To the administration of fixed dose combinations of different APIs, extended the drug product life cycle, buccal/mucoadhesive.
- For the delivery systems that should fabricate novel drug deliver systems such as chewing device and floating tablets for gastro-retentive drug delivery system.
- To control the delivery rate of either single or two different API.
- To change the all-surface area available for API layer either by sandwiching with one or two in active layers in order to create swellable/erodible barriers for modified release system.
- To separate incompatible Active pharmaceutical ingredient (APIs) from each other, to control the release of API from one layer by utilizing the functional property of the other layer (such as, osmotic property).

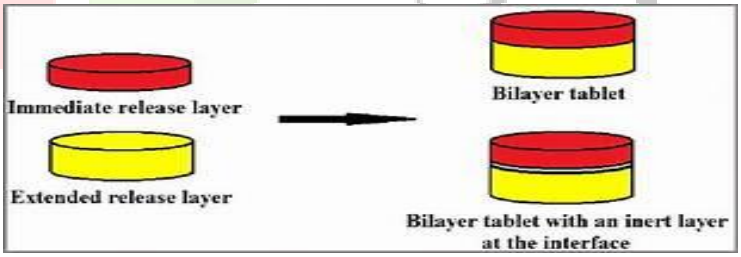

Fig.02: Bilayer Tablets

Types of Bilayer Tablet:

1. Homogenous Bilayer Tablets
2. Heterogeneous Bilayer Tablet

1) Homogenous Bilayer Tablets: When the drug release patterns differ, homogenous type bilayer tablets are the preferred option. It allows the disintegration and release characteristics to be designed and modulated. These are manufactured such that one layer provides immediate release and the other is meant to provide an extended release or second dose.

2) Heterogeneous Bilayer Tablets: A heterogeneous bilayer tablet can be used to release two drug that are incompatible or to release two medications in combination sequentially.

Advantages [1,2]

- They are used as an extension of a conventional technology.
- Potential use of single entity feed granules.
- Separation of incompatible components.
- Patient compliance is enhanced leading to improved drug regimen efficacy.
- Patient convenience is improved because fewer daily doses are required compared to traditional delivery system.
- Maintain physical and chemical stability.
- Retain potency and ensure dose accuracy

Disadvantages [3]

- Adds complexity and bilayer rotary presses are expensive.
- Insufficient hardness, layer separation, reduced yield.
- Inaccurate individual layer weight control.
- Cross contamination between the layers.

Types of Bilayer Tablet Press:

1. Single Sided Tablet Press.
2. Double Sided Tablet Press.
3. Bilayer Tablet Press with Displacement Monitoring.

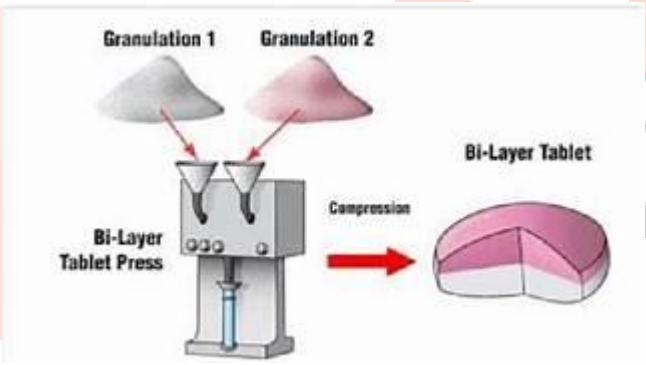

Fig.03: Bilayer Tablet Press

1) Single Sided Tablet Press:

The press design is simple and consists of a single-sided press with both chambers of the doublet feeder separated from each other. Each chamber is gravity fed or forced-fed with different power, producing two individual tablet layers. When the die passes under the feeder, it gets loaded with the first layer of powder and then subsequently by the second layer of powder. Then the entire tablet is compressed in one or more steps.

Limitations of the Single sided Press:

- No weight control/ monitoring of the individual layers.
- No distinct separation between the two layers is seen visually.
- Dwell time is very short for the first layer due to the small compression roller, which results in hardness and capping problems. Reduction in the turret- rotation speed can be done for the extension of dwell time.

2) Double Sided Tablet Press:

A double-sided press provides an individual fill station, pre-compression, and main compression for each layer. The bi-layer tablet will undergo four compression stages before being ejected from the press. Tablet weight is monitored and managed using compression force in the majority of double-sided tablet presses with automated production control. In this, the effective peak compression force exerted on each tablet or layer is measured by the control system at the main compression of the layer.

This measured peak compression force is the signal the control system uses to reject out-of-tolerance tablets and correct the die fill depth when required.

Limitations of Double-sided Tablet Press:

- Correct bonding is obtained only when the first layer is compressed at a low compression force. Because of the low compression force applied, this first layer can still interact with the second layer during final compression. But bonding gets restricted if the first layer is compressed at a high compression force.
- The low compression force required when compressing the first layer reduces the accuracy of the weight monitoring or control of the first layer.
- Bilayer tablet press with displacement monitoring: The displacement tablet weight control principle is different from the principle basedon compression force. When measuring displacement, the control system sensitivity depends on the applied pre-compression force and doesn't depend on the tablet weight.

Advantages of Double-sided Tablet Press:

- Low compression force is exerted on the first layer to avoid capping and separation of the individual layer.
- Maximum prevention of cross-contamination between two layers is achieved.
- Yield is maximized.

3) Bilayer Tablet Press with Displacement Monitoring:

The displacement tablet weight control principle is different from the principle basedon compression force. When measuring displacement, the control system sensitivity depends on the applied pre-compression force and doesn't depend on the tablet weight.

Advantages of Bilayer Tablet Press with Displacement Monitoring:

- Weight monitoring or control for the individual layers' accurate and independent weight control is achieved.
- Maximum prevention of cross-contamination between the two layers is achieved.
- Clear visual separation between the two layers is seen, and the yield is maximized.

Various Techniques for Bilayer Tablet: *[04,05,06,07,08]*

A. Oros® Push Pull Technology:

This system consists of mainly two or three layers among which the one or more layer is essential of the drug and other layer are consist of push layer. The primary consists of the drug layer are the drug and two or more different agents. So, the drugs in this drug layer are in a form that is weakly soluble. Osmotic and suspending agents have been used in addition. The tablet core is surrounded by a semi-permeable membrane.

B. L-OrosTM Technology:

This method used to the solubility problem Alza created the L-OROS system, which starts with the manufacturing of a lipid soft gel product with a medicine dissolved in it. It is then coated with a barrier membrane, an osmotic push layer, and a semi-permeable membrane that has an exit hole drilled in it.

C. DUROS Technology:

The exterior cylindrical titanium alloy reservoir is the system's main component. This reservoir shields the medication molecules from enzymes and has a high impact strength. The DUROS technology is a small medicine distribution device that functions similarly to a miniature syringe and continuously and consistently releases a little amount of concentrated form over the course of several months or years.

D. DUREDAS or Dual Release Drug Absorption System Technology:

This system is known as Elan drug technologies' Dual release drug delivery system. A bilayer tablet with DUREDAS™ Technology can deliver two medications in one dose form at varied release rates or with immediate or sustained release. Within a single tablet, the tableting technique can produce two distinct layers: a modified release hydrophilic matrix complex and an immediate release granulate. The modified-release properties of the dosage form a combination of hydrophilic polymers.

E. RoTab Bilayer:

RoTab bilayer when using is switched to production mode. Dose and compression force is automatically regulated by adjusting filling speed and die table. Hardness is also regulated when its required.

F. EN SO TROL Technology:

Shire Laboratory uses an integrated strategy to drug delivery, focused on identifying and incorporating the identified enhancer into controlled release technologies, in order to achieve solubility enhancement of an order of magnitude or to generate an optimum dosage form.

G. Geminex Technology:

This technology can greatly help increase the drug's therapeutic effectiveness and minimize its side effects. This technology is characterized by delivering one or more active substances having different drug release patterns through a single dose. It is useful to patients and pin industries as a single tablet provides drug delivery at different rates.

H. PRODAS or Programmable Oral Drug Absorption System:

It is a multi-particulate drug delivery technology based on the encapsulation of controlled release mini tablets in the size of 1.5 to 4mm in diameter this technology can be used to pre programme the release rate of a drug.it is possible to incorporate different mini tablet at difference sites within the GIT. This represents a combination of multi-particulate and hydrophilic matrix tablet technology and provide the benefit of both system in one dosage form. Such combination includes immediate release, delayed release, and controlled release minitablet.

Evaluation Studies of Gastro Retentive Bilayer Floating Tablets: *[08,09,10,11]*

In-vitro Evaluation of Bilayer Floating Tablet:

Evaluation was carried out to assess the formulations' physicochemical properties and release characteristics.

Pre-Compression Parameters:

Angle of Repose: Angle of repose is the maximum angle possible between the surface of the powder pile and the horizontal plane [height].

$$\tan \theta = h / r$$

$$\theta = \tan^{-1} h / r$$

Where θ= Angle of repose, r = radius of pile, h= height of pile.

Density: The bulk density (BD) and tapped density (TD) were determined using the following formulas,

Bulk density = weight of powder / Bulk volume

Tapped Density = Weight of powder / Tapped volume

Compressibility Index: The compressibility index of was determined by following formula,

Carr's Index % = TD-BD/ TD x 100

Hausnser's Ratio: It is calculated using the formula,

Hausner's ratio = TD / BD

Particle Size Distribution: Particle size distribution was done using the sieving method.

Post-Compression Parameters:

General Appearance: The general appearance of a tablet includes tablet's size, shape, colour, odour, taste, surface texture, and physical flaws.

Tablet Thickness: Three tablets were taken randomly, and their thickness and diameter were measured by vernier caliper or calibrated screw gauze.

Weight Variation Test: 20 tablets are selected and weighed individually. Then the deviation of individual weight from the average weight is calculated.

Hardness: The tablet's resistance to capping, abrasion or breakage under storage conditions, transportation, and handling before usage depends on its hardness. It is measured using Monsanto hardness tester by randomly selecting three tablets. It is expressed in kg/cm^2.

Friability: Friability testing is used to test the durability of tablets during packing processes and transit.

10 tablets are selected, weighed, and then placed in Roche friabilator, which rotates at 25 rpm speed for 4 min. After 4 minutes, the tablets are reweighed. Friability is calculated using formula,

$$\%F = [1-(Wt / W)] \times 100$$

W=Initial weight of tablet,

Wt= Weight of tablet after revolution.

If % Friability of tablets is less than 1%, it is considered as acceptable.

Tablet Density: It is a very important parameter in case of floating tablets. If density is less than gastric fluid (1.004), then the tablets will float. It is calculated by using following formula,

$$V = \pi r2h$$

$$d = m/v$$

r = Radius of tablet, h = crown thickness (g/cc), m = Mass of tablet.

Drug Content:

10 tablets from each batch are selected randomly and transferred to a 100 ml volumetric flask filled up with 0.1 N HCL. Stir and keep it aside for 2 hr then take 1 ml from the volumetric flask and transfer it to the test tube. Samples are then filtered, suitably diluted and analysed spectrophotometrically at a suitable wavelength.

In-vitro Dissolution Study:

The tablet was placed inside the USP paddle apparatus by maintaining an optimum temperature of 37ºC at 50 rpm rotational speed. 5 ml of sample is withdrawn at different time intervals of 1h, 2h, 3h, 4h, 5h, 6h, 8h, 10 h and 12h or any other time intervals as needed. The volume of dissolution fluid is adjusted to 900 ml by replacing fresh 5 ml of dissolution medium after each sampling. The release studies were conducted, and the mean values were plotted versus time. Each sample is analysed at maximum wavelength using UV visible spectrophotometer against a reagent blank, and the corresponding concentration is determined from the respective calibration curve. Then, the percent drug release concentration values at different time intervals were calculated.

Floating Lag Time:

Time required for the tablets to rise on the surface of the medium is floating lag time. It should ideally take less than one minute. A dissolution test device with 0.1 N HCl (900 ml) is used to measure it.

Floating Time:

The total duration of tablet floating on the medium was considered as floating time.

Swelling Study:

Weigh the tablet (W1) and place in a glass beaker, containing 200 mL of 0.1 N HCl, maintained in a water bath at 37 ± 0.5°C. At different time intervals, the tablet is removed and a filter paper carefully removes the excess of liquid. The swollen tablet is reweighed (W2).

The formula calculates the swelling index (SI),

$$SI = Wt - W0/W0 \times 100$$

Wt = weight of the swollen tablet,

W0=Initial weight of the tablet.

Stability Study (Temperature Dependent):

The bilayer tablets are stored under the following conditions for a prescribed period as per ICH guidelines for accelerated studies.

Conclusion:

In terms of both the dosage fraction and the delivery degree, the two distinct release phase approach is well-known for meeting pharmacokinetic and therapeutic requirements. In the immediate-release layer, Indion 414 has a potent effect on in vitro disintegration and in vitro drug discharge. The result of 2^3 full factorial design discovered such asthe HPMC K4M, NaHCO3 and ethyl cellulose concenetrations alluringly distress the responses, % CDR, FLT, % Swelling index and T 50%. The results showed that, if a methodical preparation approach was taken, it would be possible to obtain two medications that were taken at different dosages and therefore increase bioavailability, improve patient compliance, and restore disease control.

Acknowledgement:

I express my sincere gratitude toward management of Sudhakarrao Naik Institute of Pharmacy, Pusad for providing all obligatory facilities necessary to carry out present work. Also Prof. Dr. A. A. Harsulkar for their specialized guidance.

References:

1. Poddar SS, Abdul S; A flexible technology for modified release of drugs: multilayered tablets. Journal of Control Release, (2004); 97(3): 393– 405.

2. Liu L, Xu X; Preparation of bilayer-core osmotic pump tablet by coating the indented core tablet. International Journal of Pharmacy, (2008); 352: 225–230.

3. Martindale W, Reynolds JEF; Martindale, The Extra Pharmacopoeia. 31st edition, The Pharmaceutical Press, London, 1996: 936–937.

4. Available from URL: http://www.durect.com

5. Rahul Kumar Garg and Indrajeet Singhvi: Bilayer Floating Tablet Technology: An Overview. International Journal of Pharmacy and Pharmaceutical Research (2015); 3(3): 302- 322.

6. Gopinath C, Bindu VH and Nischala M: An overview on bilayered tablet technology. Journal of Global Trends in Pharmaceutical Sciences (2013); 4(2):1077-1085.

7. Satpute VM and Tuljapur NT: Bi-layer tablet: A controlled release dosage form. International Journal of Research and Analytical Reviews (2020); 7(1): 330-343.

8. Pujara ND, Gokani RK and Paun JS: Bilayer tablet-an emerging trend. International Journal of Pharmaceutical Research and Development (2012); 4(4): 103-111.

9. Singh LP, Rajesh KS, Umalkar DG, Chauhan VK, Rana VK and Vasava KS: Floating effervescent tablet: A review. Journal of Pharmaceutical and Biomedical Sciences (2011); 5(11): 1-6.

10. Pethkar SV, Suggala V, Gholap S, Salunke R, Jain H and Swain K: Review on: Bilayer Floating Tablet. World Journal of Pharmacy and Pharmaceutical Sciences (2016); 5(2): 1411-1423.

11. Rao SV, Priyanka B and Padmalatha K: Bilayer tablet technology: A novel approach. GSC Biological and Pharmaceutical Sciences (2019); 7(2): 22-28.

12. KAUSHIK SAINI, NAVNEET VERMA, GAURAV KUMAR, (2020), REVIEW ARTICLE OF FLOATING TABLET BY NATURAL AND SYNTHETIC POLYMERS, IJCRT | Volume 8, Issue 11 November 2020 | ISSN: 2320-2882.

13. MD. Afrose soha and P. Veera Lakshmi, (2021) A REVIEW ON FLOATING DRUG DELIVERY SYSTEM, ISSN: 2231–2781, IJRPC 11(4), 118-127.https://dx.doi.org/10.33289/IJRPC.12.10.2021.11(41).

14. Baviskar P, Patil P and Saudagar RB. Floating Drug Delivery System: A comprehensive review, Journal of Drug Delivery and Therapeutics. (2019); 9(3-s):839-846. http://dx.doi.org/10.22270/jddt.v9i3- s.2945.

15. Shinde Jitendra V, Malshikare Swapnali S and Chavanrajashree S. A Review on Floating Drug Delivery System. Published in International Journal of Trend in Scientific Researchand Development (ijtsrd). (2020);4(3):427-433.

16. Iyan Sopyan, Sriwidodo, Retno Wahyuningrum and Norisca Aliza P. A review: Floating drug delivery system as a tool to improve dissolution rate in gatric. Int J App Pharm. (2020);12(4): 51-54.

17. Vijay Sharma, Rathore DS and Amit Kumar. Floating drug delivery system. A review International Journal of Medical and Biomedical Studies (IJMBS). (2020);4(8):23-30.

18. Geetha A, Kumar JR, Mohan K and Sateesh V. A Review on Floating Drug Delivery Systems. Int J Pharm Res. Biomed. Anal. (2012).

19. Chikhalikar SS and Wakade RB. Floating Drug Delivery System – An Approach to Oral Controlled Drug Delivery. International Journal of Pharm Tech Research. (2012);4(4):1812-26.

20. Jegadeesh Nagigoti and Shayeda. Floating Drug Delivery System. Int J Pharm Scien Nano. 2009;595-601. 8. Majethiya KA and Patel MR. Review on: Gastro retentive Drug Delivery System. International Journal of Universal Pharmacy and Bio Sciences. (2010);2(1):103-120.

21. Srivastava a.k, wadwa s. Oral sustain delivery of atenolol from floating matrix tablets and invitro evaluation, drug. Dev. Ind. Pharm., (2005): 31(45); p.367-374.

22. Alam, p., mk anwer, and ma ghanie. "Development and evaluation of gastroretentive floating tablets of ginger extract: antiulcer activity". (2014); 3(11): 2455-2465.

23. B.B. Alsulays, V. Kulkarni, S.M. Alshehri, B.K. Almutairy, E.A. Ashour, J.T. Morott, A.S. Alshetaili, J.B. Park, R.V. Tiwari, M.A. Repka, Preparation and evaluation of enteric coated tablets of hot-melt extruded lansoprazole, Drug Dev. Ind. Pharm. (2017).

24. B. Maddiboyina, V. Jhawat, G. Sivaraman, O.P. Sunnapu, R.K. Nakkala, M.H. Naik, M. Gulia, Formulation Development and Characterization of controlled release core in cup matrix tablets of venlafaxine HCl, Curr. Drug Ther. (2020).

25. K Palsamy SA Mookkandi, G. Sivaraman, B. Maddiboyina, J. Annaraj, J. Rajesh, R. Gurusamy, A novel curcumin-loaded PLGA micromagnetic composite system for controlled and pH-responsive drug delivery, Colloid. Surface. Physicochem. Eng. Aspect. (2019).

26. T. Muinao, H.P.D. Boruah, M. Pal, Current advances on polysaccharide-based nanoconjugates for efficient and targeted drug delivery in cancer treatment, in: Polysacch. Carriers Drug Deliv, (2019).

27. NCD Risk Factor Collaboration (NCD-RisC), Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants, Lancet (2017).

28. Maniya shrikant, Shreeraj shah, Pratik Upadhay. Floating bilayer drug delivery system- An unconventional approach in convetional form. Am.J. PharmaTech Res, 2(2), (2012), 609-628.

29. Satinder Kakar, Deepa Batra, Ramandeep Singh, Ujjwal Nautiyal. Magnetic Microspheres as Magical Novel Drug Delivery System: A review; Journal of acute disease 2013:1-12.

30. Balaji G, Prakash GK, Suresh K and Venkatesh B. Bilayer tablet are view. IJRRPAS. (2013);3(4):488-506.