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Floating Tablet: An Approachable Tool for Drug Delivery System of Floating Tablet of Telmisartan for the Management of Hypertension

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ABSTRACT:
Nanotechnology holds a productive potential about to happen explored as a multifunctional word of light at end of tunnel for a wide alps of biological and engineering applications a cleanly known as molecular sensors for money under the table diagnosis, therapeutic agents for the service of diseases, and a gadget for delivering therapeutics and imaging agents for theranostic applications in cells and income animals Nanotheranostics is a burgeoning employment in natural years, which makes consider of "nanotechnology" for diagnostics and attitude of contradictory diseases. The recent climbing the corporate ladder in the objective of nanotechnology has enabled a new birds and the bee of diverse types of nanomaterials balanced of as a substitute inorganic or polymer based nanoparticles to be satisfying for nanotheranostics applications. Some of the notable features of the nanotechnology towards science of the mind are cost slump, dependable detection and diagnosis of diseases at an quickly stage for optimal treatment.

Keywords: Nanotechnology, Drug targeting, Molecular biomaterials, Molecular imaging, Oral chemotherapy, Pharmaceutical nanotechnology.

INTRODUCTION

The aim of Floating Drug Delivery System is to afford a therapeutic amount of Drug to proper site in the body for the achieve better plasma drug concentration to desired period of time .So the major principle of Floating delivery is increase the gastric retention time and improve Bioavailability. This system are based on hydrodynamitically balanced system for better patent compliance to take dose once in a day to treat Hypertension .FDDS are most important Drug delivery system in novel drug delivery system .Reduce dosing frequency are very important factor for floating delivery to achieve good bioavailability of drug. Sometimes the physiological parameters are also affected the gastrointestinal tract environment as well as depends on its pH. So these kinds of parameters affected gastric residence time .So that finally this floating system can be totally overcome to these difficulties during the dose administration and pharmacokinetics, Dynamics parameters related to overall process of dose. The controlled Gastric Retention of solid dosage form may be mainly achieved by mucoadhesion ,Floatation or some time sedimentation according to used their polymers or excipients of their formulation variability .Plasma Drug Concentration mainly attain by the floatation lag time period is their advantage of Floating Drug Delivery system .This Delivery system can remain in the

stomach for prolong time and enhance GRT of numerous drugs .In this system advantages beneficial to drug that show low solubility at high pH. This system reduces instability of gastric wall. Drug polymer compatibility studies are very important to responsible for interaction activity. Total floating time or floating lag time are high in this delivery system for the beneficial of floatation of dosage form solid or mucoadhesive. Its main major target of enhance bioavailability and increase retention time for the better patent compliance.

Mechanism of Floating Drug Delivery System:

Floating drug delivery System is the Low Density System. This system have a sufficient buoyancy to float over the gastric contents to remain in the stomach for long period of time .Floating dose to float over the gastric contents and release slowly at the desired rate of action .So the result is found increased Gastric retention time and improve Bioavailability and reduces Fluctuation. Those system advantages is very less amount of gastric content is required to achievement of buoyancy retention principal.

Anatomy and Physiology of Gastrointestinal tract: Stomach is divided anatomically in 3 parts: Funds, Body, Antrum (Pylorus). The proximal part is made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions.

Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phases as described by Wilson and Washington.

Table 1:

Phase	Time	Comment
Phase I (Basal phase)	Last for 30 to 60 minutes	Rare contractions
Phase II (Pre Burst phase)	Last for 20 to 40 minutes	Immediate contract ions, as phase progress intensity & frequency also.
Phase III (Burst phase)	Last for 0 to 5 minutes	Intense and regular contract ion occurs during this phase for short period of time
Phase IV	Last for 10 to 20 minutes	Between phases 1 to 2

After the ingestion of a uniform meal, the pattern of contractions changes from fasted to that of fed state. This is also known as digestive motility pattern and comprises unremitting contractions as in phase II of fasted state. These contractions result in tumbling the size of food particles (to less than 1 mm), which are propelled in the direction of the pylorus in a suspension form. During the fed state onset of MMC is belated resulting in reduce speed of gastric emptying rate.

Factors Effecting Gastric Residence Time: Gastric dwelling times of floating tablets are improved and prolong gastric time but some factors can be affected the gastric surroundings its depends on different anatomy and physiology variations of humans.

1. Nature of Meal: This factor can be affected the gastric residence time .Feed and indigestible polymer or fatty acids can be change gastric motility that is the reason is decreasing the gastric emptying rate.

2. Caloric content of meal: Gastric residence time can be enlarged by the 3 to 9 hrs approximately with the meal of high protein and high fatty acids content meal .SO the high caloric meal are effected indigestion and delay emptying time of stomach

3. Volume of G.I Fluid: The sleeping volume of stomach is low aprox 25ml to 50 ml.When the volume is large, the emptying is faster.

Dosage Form Related Factors:

Density: Gastric retention time (GRT) is a purpose of dosage form optimism that is dependent on the density.

Size: Dosage form units with a diameter of more than 7.7 mm are reported to have an improved GRT compared with those with a diameter of 9.8mm.

Shape of Dosage Form: tetrahedron and ring shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better GRT 88% to 100% retention at 24 hours compared with other shapes.

Single or Multiple Unit Formulation: Multiple unit formulations show a more conventional release profile and insignificant impairing of presentation due to failure of units, allow co-administration of units with different release profiles or contain unsuited substances and permit a better periphery of safety against dosage form failure compared with single unit dosage forms.

Fed or Unfed State: Under fasting conditions, the GI motility is characterized by periods of physically powerful motor activity or the migrating myoelectric complex (MMC) that occurs every 1 to 2 hours. The MMC sweeps undigested bits and pieces from the stomach.

Frequency of Feed: The GRT can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC.

Gender: These factors are also important in gastric emptying time delay just because of male and female patents and all other regardless of the weight, height and body surface).

Age: Elderly people, especially those over 70, have a significantly longer GRT.

Posture: GRT can vary between supine and upright ambulatory states of the patients.

Classification of Floating Drug Delivery Systems (FDDS):

(A) Effervescent FDDS
- Gas generating system
- Volatile liquid containing system

(B) Non- Effervescent FDDS
- Colloidal gel barrier system
- Micro porous compartment system
- Floating microsphere
- Alginate floating beads.
- Raft forming system

Effervescent System

The floating systems are arranged with swellable polymers such as methocel or polysaccharides like hydroxyl propyl cellulose, Carbopol, HPMC and effervescent component containing sodium bicarbonate, citric and/or tartaric acid or matrices containing chambers of liquid that gasify at body temperature. The matrices are fictitious so that contact with gastric fluid, carbon dioxide is evolved by the acidity of gastric contents and is entrapped in the gelyfied hydrocolloid.

(1) Gas Generating System: These systems are low density FDDS is based on the formation of evolved co2 within the device following contact with body fluids. The resources are fictitious so that upon influx in stomach, co2 is evolved by acidity of the gastric content and is entrap in the gellified hydrocolloid produce

uphill movement of the dosage form and uphold its buoyancy.

(2) Osmotically Controlled Floating System: As an Volatile liquid containing floating system, the mechanism comprise of a consecrate deformable estranged by a water-resistant, pressure receptive changeable bladder. The first chamber contain an active drug, while the second chamber contain a volatile liquid, such as cyclopentane or ether that vaporises at physiological temperature to fabricate a gas, enabling the drug reservoir to float.

(B) Non-Effervescent FDDS

Non-Effervescent FDDS use a gel forming (or) swellable cellulose type polymer of hydrocolloid, Polysaccharide, matrix forming polymer like polycarbonate, polymethacrylate and polystyrene. One of the formulation methods involves the mixing of the drug with gel forming hydrocolloids which swell in contact with gastric fluid after oral administration and maintains integrity of shape and a bulk density barrier, the air trapped by swollen polymer confer buoyancy to the dosage forms.

a) **Colloidal Gel Barrier System** :Colloidal barrier system are also known as the Hydrodynamically balanced system .This system contains drug with gel carrier system provided to remain long period of time in stomach without any unstability on gastric wall .Prolong duration of time and increase Gastric Residence time of drug for high plasma drug concentration reaches in blood.This gel barrier system made up of included gel forming agent like that highly soluble cellulose type hydrocolloid e.g.(HPMC),polysaccharides and matrix forming polymer such as polycarbophil, polystyrene and polyacrylate.

b) **Microporous Compartment System**: This expertise is based on the encapsulation of a drug reservoir inside a Microporous compartment with pores along its top and bottom walls. The marginal wall of the drug reservoir compartment is entirely preserved to foil any direct contact of gastric surface with the undissolved drug. In the stomach, the floatation chamber containing entrapped air causes the floatation chamber containing entrapped air causes the delivery system to float over the gastric content.

c) **Floating Microspheres:** Sanctify microspheres are considers as most shows potential buoyant system as they are more useful because of middle hallow space inside the microsphere.

d) **Alginate Floating Beads:** Multi-unit floating dosage forms have been developed from freeze calcium alginate Spherical beads of approximately 2.5 to 3 mm in diameter can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride using syringe with needle for the spheriacal droplets of sodium alginate beads. Causing the precipitation of calcium alginate. The beads are than separated, snap-frozen in liquid nitrogen and freeze-dried at 400C for 24 hrs. Then kept on a desicator for the drying purpose .So prepared beads are ready for evaluation.

C. Raft Forming System : Propel forming system have customary much attention for the delivery of antacid and drug Delivery for gastro infection and disorders on contact with gastric fluid a gel forming Solution swells and forms a gelatinous consistent gel containing entrapped co2 froth. Which Forms propel layer on top of gastric fluid which releases drug slowly in stomach. (Often used

For gastro esophageal reflux treatment.Raft forming system are very important for the floating drug delivery system.

Advantages of FDDS:

1. **Sustained drug delivery**: Floating drug dosage forms can remnants in the stomach for make longer time and improve the GRT of frequent drugs

2. Site-specific drug delivery: These drugs such as furosemide, riboflavin show site specific absorption in the upper part of GIT. Those drugs used for take once in a day.

3. Local action in stomach: The FDDS are advantageous for drugs that are aspiration to generate local action in the stomach. For example: antacids.

4. Reduce irritation of acidic drugs: Acidic drugs, after administration may cause irritation on the stomach wall. So these systems are avoided and remove irritation of acidic drugs on the gastric wall.

5. Advantageous to drugs which are unstable in intestine environment: Sometimes those drugs are caused unstability in intestinal environment Drugs such as Captopril, ranitidine HCl, metronidazole which are unstable in the intestinal or colonic environment can be administered by assembly floating dosage forms.

6. Beneficial to drugs that show low solubility at high pH: These drugs such as diazepam, chlordiazepoxide, verapamil show low solubility at high pH. FDDS can be because it enhances the GRT of these drugs and hence raise the bioavailability of these drugs by achieve better absorption.

7. Pharmacokinetic advantages: FDDS retain constant blood level because of sustain released nature of these dosage forms, easy to administration and better patient compliance is provided by this.

8. Reduce frequency dosing

9. Improved Bioavailability

10. Reduce fluctuation of drug concentration

Limitations:

1. Floating system requires high level of fluids in stomach for floating and sufficient buoyancy efficiently, so extra water intake is given with this type of dosage form.

2. In supine condition (like sleeping posture) floating dosage form may swept away by contractile bearing. So patient should not take floating dosage form just before going to bed.

3. Food is also an imperative factor existence of food delays emptying time of food and dosage form. So presence of food is preferable.

Approaches to Increase Gastric Retention:

The following approaches have been studied to improve the retention of an oral dosage for in the stomach. Examples:

1. Floating System

Floating drug delivery systems (FDDS) have a volume density a reduced amount of than gastric fluid and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. Floatation of a drug delivery system in the stomach can be achieved by incorporating floating chamber filled with vacuum, air, or inert gas.

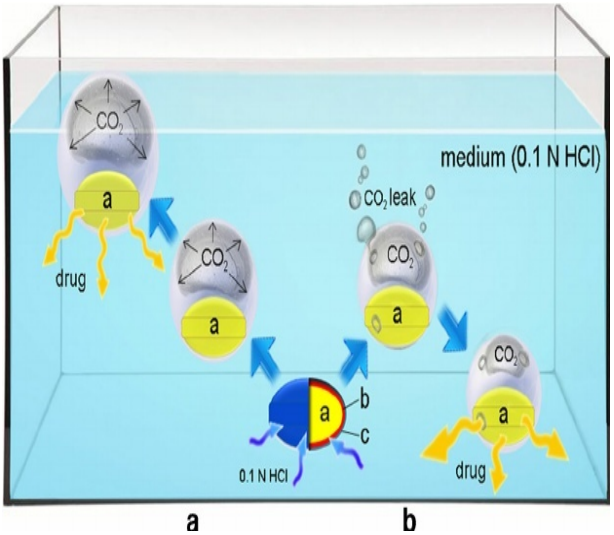

Fig. 1.1: Floating System of Tablet in G.I Tract

2. Mucoadhesive and Bioadhesive System

Bioadhesive drug delivery systems are used to localise a delivery device within the lumen to enhance the drug absorption in a site specific manner. This type of approach participate in the use of bioadhesive polymers, which can

adhere to the surface of epithelial in stomach. Some of the mainly capable excipients that have been used commonly in these systems include polycarbonates, carbopol, mucoadhesive lectins , chitosan, CMC and HPC etc

3. High Density System

These systems, which have a density of ~3.5g/cm3, are remain in the rogue of stomach and capable of outstanding performance in the gastric content . High density system is most preferable system in this system.

1. Single-unit Dosage Forms

Low-density Approach: This approach, the globular shells with density lower than that of gastric fluid can be used as carrier for drug for making single-unit floating dosage form. Telmisartan drug are used for low density system to take once in a day in 24 hrs.

Fluid- filled Floating Chamber: Fluid filled floatation chamber are very necessary for the floatation of drug just because of high fluid are required for the dose administration oral or other routes of administration ,In this type of dosage forms, a gas-filled floatation chamber is built-in into a microporous element that cover the drug chamber . beside the top and bottom walls there are stipulation for opportunity through which the GIT fluid enters into the dissolve drug matrix reservoirs.

Hydrodynamically Balanced Systems (HBS): These systems enhance high plasma drug concentration then achieve absorption because they are planned such that they hang about in GIT for make longer time. Drugs which have a enhanced solubility in acidic environment and site-specific absorption in the upper part of GIT for such systems.

Preparation of Floating Tablets:

Telmisartan floating tablets were formulated wet granulation method. The formulation composition of different batch is shown in Table 1. All the powders passed through 40 mesh sieve. The required quantity of telmisartan, various polymers and fillers were mixed thoroughly. And prepare 10% polyvinyl-Pyrrolidone solution in isopropyl-alcohol for the wet mass prepared to granules pass through 18 mesh size sieve. Granules kept in Trayed Dryer for 1 hrs.after the drying of granules pass through 16 mesh size sieve. Magnesium stearate and talc were finally added as a lubricant and Guidant respectively. The granules are directly compressed (8 mm diameter, circular flat faced punches) on a rotary tablet punching machine. Each tablet contained 60 mg of telmisartan. All the tablets were stored in airtight containers for further study.

4. Conclusions

FDDS promises to be a prospective advance for gastric retention. Number of profitable products and patents issued in this field are the evidence of it. The aim is to improve the bioavailability of the drug with contracted absorption window in gastrointestinal tract region. By prolonging the drug resident time in GI region improves the bioavailability of drug that is less soluble in high PH and reduces drug waste, reduction in plasma level fluctuation. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

References

1. Alvisi V, Gasparetto A, Dentale A, Heras H, Felletti Spadazzi A, Ambrosi AD. Bioavailability of a controlled release formulation of Telmisartan hypertension. *Drugs Exp. Clin. Res,* 22, 1996, 29–33.
2. Abhishek Chandel, Kapil Chauhan, Bharat Parashar, Hitesh Kumar, Sonia arora Floating drug delivery systems: A better approach , Chandel et al., International Current Pharmaceutical Journal 2012, 1(5): 110-118.

3. A.A Deshpande, N.H Shah, C .T Rhodes and W.Malick (1997). Pharm.Res: Vol.14 815-819.

4. Arora Shweta, Javed Ali, Ahuja Alka, KharRoop K and Baboota Sanjula, "Floating Drug Delivery Systems: A Review." AAPS Pharm SciTech 2005; 6 (3) Article 47.

5. Babu VBM, Khar RK. In vitro and In vivo studies of sustained release floating dosage forms containing salbutamol sulphate. Pharmazie 1990; 45: 268-270.

6. Bhardwaj V, Nirmala SL, Harikumar, "Floating Drug Delivery System: A Review", *Pharmacophore.* **2013**, 4(1): 26-38.

7. Burns SJ, Attwood D, Barnwell SG. Assesment of a dissolution vessel designed for use with floating and erodible dosage forms. Int J Pharm 1998; 160:213-218.

8. Baumgartner, S., Kristl, J., Vreˇcer, F., Vodopivec, P., Zorko, B., 2000. Optimisation of floating matrix tablets and evaluation of their gastric residence time. Int. J. Pharm. 195, 125–135.

9. Chikhalikar S.S, Wakade R.B. Floating Drug Delivery System – An Approach to Oral Controlled Drug Delivery International Journal of Pharm Tech Research Vol.4, No.4, pp 1812-1826, Oct-Dec 2012.

10. Chavanpatil, M.D, Jain P, Chaudhari, S, Shear R, Vavia, P.R., 2006. Novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin. Int. J. Pharm. 316, 86–92.

11. Davis, S.S Hardy, J.G, Taylor, M.J, Whalley, D.R, Wilson, C.G, 1984. A comparative study of the gastrointestinal transit of a pellet and tablet formulation. Int. J. Pharm. 21, 167-177.

12. Dave BS, Amin AF, Patel M. Gastrorentive drug delivery system of ranitidine HCl formulation and in vitro evaluation. AAPS Pharma Sci Tech 2004; 5:1-10.

13. Deshpande A A, Rhodes CT, Shah NH, Malick AW. Controlled release drug delivery system for prolonged gastric residence: An overview. Drug Delivery Ind pharm, 22:, 1996, 331-340.

14. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-release system for gastric retention. *Pharm. Res,* 14, 1997, 815–819.

15. Desai S. A Novel Floating Controlled Release Drug Delivery System Based on a Dried Gel Matrix Network [master's thesis]. [Thesis]. Jamaica, NY: St John's University 1984.

16. Desai S, Bolton S. A floating controlled release drug delivery system: in vitro- in vivo evaluation. Pharm Res 1993; 10:1321-1325.

17. Grubel P et al. Gastric emptying of nondigestible solids in the fasted dog. J Pharm Sci, 76, 1987, 117 –122.

18. Hetal N, Kikani A. Thesis on, Floating Drug Delivery System, The North Gujarat University, Patan. 2001; 11-12.

19. KK Muraleedhar, Mohammad Ali, S Parthiban, SK Senthilkumar. floating drug delivery system: a scientific view International Journal of Advanced Pharmaceutics Vol 3 , Issue 1 2013 12-19.

20. Joseph NJ, Laxmi S, Jayakrishnan A. A floating type oral dosage form for piroxicam based on hollow microspheres: in vitro and in vivo evaluation in rabbits. J Control Release 2002; 79:71-79.

21. Kumar S, Jamil F, Rajput M, Sharma S, "Gastro Retentive Drug Delivery System: Features and Facts", International Journal of Research in Pharmaceutical and Biomedical Sciences. 2012,3(1) :125-136.

22. Mayavanshi AV, Gajjar SS, "Floating drug delivery systems to increase gastric retention of drugs: A review", RJPT. 2008, 1, 345-348.

23. M. Uddin , P. B. Rathi, A. R. Siddiqui, A. R. Sonawane, D. D. Gadade . Recent Development in Floating Delivery Systems for Gastric Retention of Drugs Asian Journal of Biomedical and Pharmaceutical Sciences 1 (3) 2011, 26-42.

24. Ozemir N, Ordu S, Ozkan Y. Studies of floating dosage forms of Frusemide: In-vitro and in-vivo evaluation of bilayer tablet formulation. Drug Dev Ind Pharm, 26, 2000, 857-866.

25. Olga C. Lastra , Igor G. Lemus, Hugo J. Sa´nchez, Renato F. Pe´rez .Development and validation of an UV derivative spectrophotometric determination of Losartan potassium in tablets Journal of Pharmaceutical and Biomedical Analysis 33 (2003) 175- 180.

26. Rajesh Asija, Sangeeta Asija, Shailendra Bhatt, Deepak Sharma, Avinash Shah and Priyanka Sharma Formulation and evaluation of floating tablet of Valsartan Journal of Chemical and Pharmaceutical Research, 2015, 7(2):708-715.

27. Rubinstein A and Friend DR. Specific delivery to the gastro intestinal tract, in: Domb A. J(Ed), Polymeric site specific pharmacotherapy. Wiley Chichester, 1994, 282-283.

28. Sawicki W. Pharmacokinetics of verapamil and nor verapamil from controlled release floating pellets in humans. Eur J Pharm Biopharm 2001; 53: 29-35.

29. Sheth PR and Tossounian JL. U.S. Patent no.4140755, 1979.

30. Stops F, Feli JT, Collett JH, Martini LG, Sharma HL, Smith AM et al. Critric acid prolongs the gastro-retention of a floating dosage form and increase bioavailability of Losartan in the fasted state. *Int J Pharm,* 308, 2006, 14-24.

31. Shiv kumar Garg, Kenganora Mruthunjaya, Manish Kumar Gupta1 & Bharat Parashar. Stomach Specific Floating Drug Delivery System: Current Approchases Asian Journal of Biochemical and Pharmaceutical Research *Issue 1 (Vol. 2) 2012.*

32. Shalini Sharma , Mukesh Prashar1, Ram Kumar Sahu . floatig drug delivery system: incredible revolution *Pharmacology online* 3: 1039-1054 (2011).

33. Kamalakkannan V, Puratchikody A, Prasanth VV and Masilamani K: Enhancement of Drugs Bioavailability by Floating Drug Delivery System – – A Review. International Journal of Drug Delivery 2011; 1: 558-70.

34. Suryawanshi A and Hiremath SP: Floating Drug Delivery System – A Review. American Journal of Pharmatech Research 2011; 2(1): 138-53.

35. Shubhrajit M, Thilothama LR and Shoshanna D. Formulation and in vitro evaluation of metoprolol succinate floating tablets by using two viscosity grade of HPMC. International Journal of Pharmaceutical Science and Research 2012; 3 (9): 3507-13.

36. Narang N: AN Updated Review On: Floating Drug Delivery System (FDDS). International Journal of Applied Pharmaceutics 2011; 3(1): 1-7.

37. Gastro Retentive Drugs: A review, Express Pharma Pulse, Apr 17 (2003).

38. Gattani YS, “Floating drug delivery system: A Review”, Int. J. Pharm. and Bio Sciences 2010, V1 (2).

39. Shah SH, Patel JK, Patel NV, “Stomach specific Floating drug delivery system: A Review”, Int. J. Pharm. Res., 2009, 3, 623-633.

40. Jain A: New Concept: Floating Drug Delivery System. Indian Journal of Novel Drug Delivery 2011; 3(3): 163-69.