IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

FLOATING DRUG DELIVERY SYSTEM: A REVIEW

Ms. Arti Devi
*** Mrs.Yugma desai**

ABSTRACT: Floating drug delivery system is recent approach for enhancing retention time of drug in stomach for their action. Floating drug delivery system is suitable for drugs which have poor bioavilability in intestinal fluid. The drug remain buoyant in the stomach. Based upon buoyancy mechanism floating drug delivery system is divided into two types, effervescent and non effervescent floating drug delivery system. In effervescent floating system co_2 gas release, system density reduce and remain buoyant in stomach. Non effervescent floating system based on polymer swelling mechanism. The drug released gradually in stomach with desired rate. Floating drug delivery system increase absorption of drug which are soluble only in stomach.

Keywords: Floating drug delivery system, Types,Mechanism, Advantages and Disadvantages.

INTRODUCTION

Nowadays the performance of controlled release can be improved with the help of gastro-retentive dosage form. [1]. First of all, the concept of float was given by Davis in 1968 after he saw someone throttled while taking medicinal pills so, that scientist propose that the problem could be solved by gastroretentive in gastro-intestinal fluid.[2,3].Drug consumption by oral route is the common method of drug administration[4]. Because of limited absorption of drug in upper part of GIT the gastro retentive drug delivery system is best for drugs with poor bioavilability[5]. In order to control these complication many drug with prolonged retention time has been developed[6,7]. One of which is floating drug delivery system. The floating drug delivery system is invented for drugs with poor bioavilability in intestinal fluids ,by this method drug retain in stomach [8]. Gastro-retentive system can endure for multiple hours in the gastric region and lengthen the gastric residence time of drug[9,10]. Gastric residence time of drugs achieved by mucoadhesion[11,12], flotation[13] and expansion[14,15]. Floating system are low density system that have sufficient buoyancy to float over the gastric content and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time[16]. This results increased gastric residence time and have a better control of fluctuation in plasma drug concentration[17,18].

PHYSIOLOGY OF STOMACH

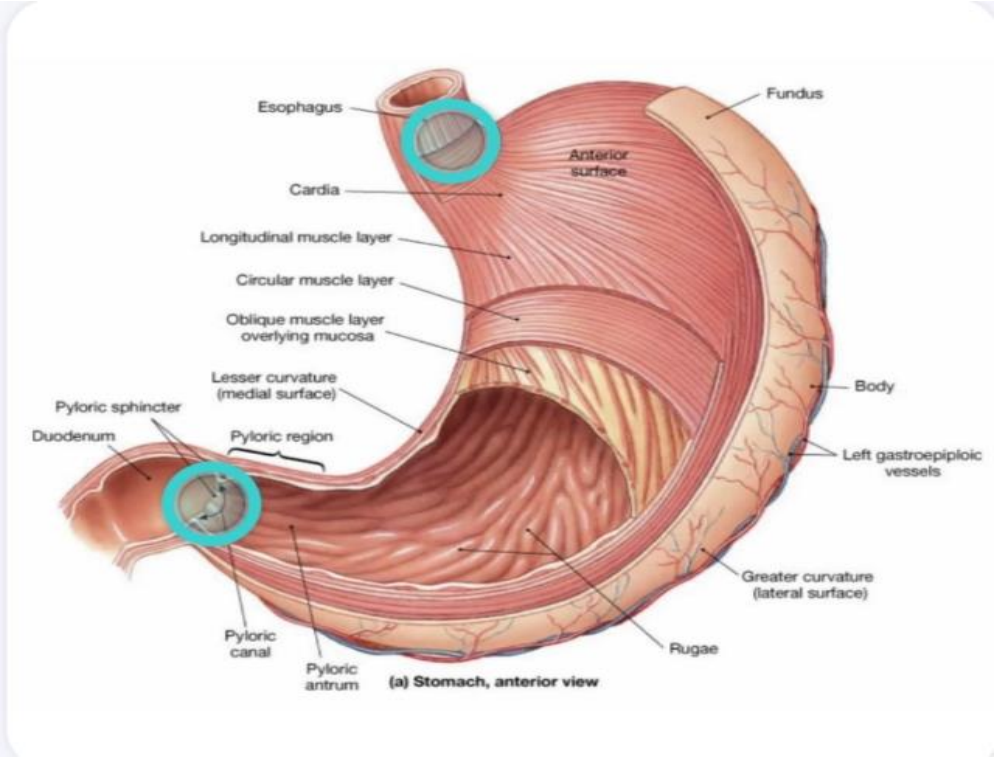

Fig. Stomach physiology

The stomach is divided into three parts fundus, body and antrum(pylorus)[19,20,21]. The proximal stomach consist of fundus and body region which act as a resevior for undigested material on the other hand distal region i.e antrum is major location for mixing motion which function as a pump for gastric emptying [22]. Stomach is an expanded digestive organ lie between oesophagus and small intestine .Contraction occur in empty stomach where . mucosa and submucosa are thrown into marked folding called **rugae.**

Major four type of secretary epithelial cells are found

Mucous cells: secrete alkaline mucus.

Parietal cells: secrete HCL.

Chief cells: secrete pepsin.

G cells: secrete hormone gastrin[23].

GI MOTILITY PATTERN

Divided into 4 phases

Phase I(basal phase): continue from 30 to 60 minutes with occasional contraction.

Phase II(preburst phase): continue for 20 to 40 minutes with periodic action potential and contraction. The intensity and frequency increases slowly as phase rise.

Phase III(burst phase): continue for 10 to 20 minutes. Regular and extreme contraction occur in this phase for short period. Undigested material is cleared out from stomach to small intestine because of this wave. Another name of this wave is housekeeper wave.

Phase IV: continue for 0 to 5 minutes and occurs between phases III and I of two consecutive cycles[24].

To transport drug in stomach various polymer used in floating drug delivery system. Example of polymers the polymers are alginic acid ,gellan gum and guar gum .Synthetic polymers are HPMC and poly caprolacton. The dosage form and retention time affected by motility pattern[25].

TYPES OF FLOATING DRUG DELIVERY SYSTEM

Floating drug delivery system based on the buoyancy mechanism is classified into two types

(A) Non-Effervescent FDDS
(B) Effervescent FDDS

(A) Non-Effervescent FDDS

The Non-effervescent floating drug delivery system works on the mechanism of swelling of polymer or bioadhesion to mucosal layer in GIT[26,27,28].Most frequently used excipitents in these systems are hydroxyl propyl methyl cellulose (HPMC), polyacrylate polymers, polyvinyl acetate, carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates[29,30].Mixing of polymer and drug is done and generally administered in a gelatine capsule. The dissolution of capsule fastly occur in gastric fluid and floating mass will be produced by hydration and swelling of surface polymers. By formation of hydrated boundary at the surface releasing of drug will be controlled[31].

The various types of Non-effervescent FDDS are:

(1). Colloidal gel barrier system

The hydro dynamically balanced system was first designed by 'Sheath and Tossounian'[32]. Drugs in these types of system consist of gel forming hydrochloride that remain buoyant on stomach content. Result prolong GRT and drug that reaches its absorption sites in solution form its amount maximizes. A high level of one or more gel-forming highly soluble cellulose type hydrocolloids are included in this system, e.g. hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropyl methyl cellulose(HPMC), matrix forming polymers like polycarbophil, polyacrylate and polystyrene and various polysaccharides[33].

(a). Single Layer Floating Tablets

The formulation is done by intimate mixing of drug and gel forming colloids and swelling occur when they are comes in contact with gastric fluid and keeping its bulk density less than unity[34]. The formulation is done by intimate mixing of drug and low density enteric material such as HPMC.

(b). Bi-Layer Floating Tablets

In bi-layer floating system two layers are present (1) immediate release layer (2) sustain release layer. Through rapid release layer the drug is released in the stomach[35]. A good product identity in a bilayer tablet which are free from defects like chips crack discoloration and contamination[36].

(2). Alginate Beads

Freeze dried calcium alginate are used formation of multi unit dosage form. Sodium alginate solution in aqueous solution of calcium chloride using dropping method can be used for preparation of spherical beads of diameter 2.5nm[37]. GRT prolonged with the help of these beads for more than 5.5 hours[38].

(3). Hollow microspheres /Microballons

Novel emulsion solvent diffusion method used for preparation. At 40^{o}c the drug solution of ethanol/dichloromethane and a polymer which is enteric acrylic is transformed into the agitated solution of polyvinyl alcohol[39,40]. Due to evaporation of dichloromethane gas phase is produced in the dispersed polymer droplet which is created in the inner cavity of microsphere of polymer and drug, continual floating of microballons onthe surface of an acidic dissolution media which contain surfactant for more than 12h[41].

(4). Micro porous compartment system

In this technology encapsulation of a drug reservoir inside a microporous compartment with pores along its top and bottom walls[42]. To stop direct contact of gastric mucosal surface the peripheral of drug reservoir compartment are fully sealed. The drug dissolved in gastric fluid which is pass through openings and convey the dissolved dissolved drug for continuous transport across the intestine for absorption[43].

(B). Effervescent FDDS

Gas generating agents, carbonates and other organic acids used in effervescent system to produce carbon dioxide (co_2) gas, as a result density of system reduce so, it float on gastric fluid[44]. Swellable polymers e.g methylcellulose and chitosan and other effervescent compounds such as sodium bicarbonate, tartaric acid and citric acid are used in this matrix type of system[45].

The effervescent system is further classified into two types

(1) Gas generating systems

(2) Volatile liquid/ vaccum systems

(1) Gas generating systems

(l). Intra gastric single layer floating tablets or Hydrodynamically balanced system (HBS): They are frequently developed by intimate mixing in the matrix tablet, the co_2 give rise to operatives and drug. The bulk density of such tablets is less than gastric electrolytes, therefore remain floating in stomach for a prolonged period of time not appealing the rate of gastric emptying. The drug in floating system is released slowly at required rate along with residual process is evict from stomach after comprehensive discharge [46].

(ll). Intra gastric bilayer floating tablets: Below figure:

Are also called as compressed tablets containing two layers

Sustained release layer and immediate release layer.

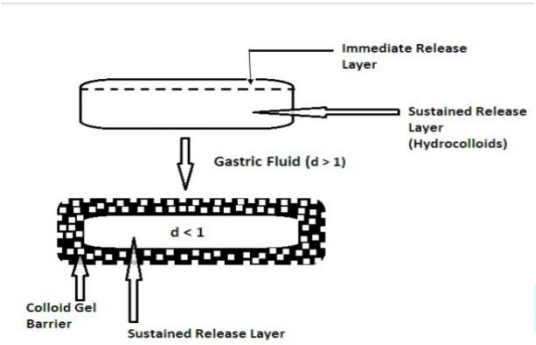

Fig. Intra gastric bilayer floating tablets

(lll). Multi unit type floating pills: Multiparticulate dosage forms acquire more favour over single-unit dosage forms[48]. In single unit formulation the main problem like sticking together or obstruction produced in gastrointestinal tract cause irritation. Multiple unit systems preventing `all-or-none' gastric emptying nature of single unit dosage unit systems, lower the chances of dose dumping and lower intersubject variabilityin absorption[49].

(2). Volatile liquid/vaccum system

(l). Intra gastric osmotically controlled floating delivery systems: This system composed of two parts, a drug reservoir compartment and osmotically active compartment. A collapsible bag present in this formulation with the help of pressure, the drug reservoir compartment is enclosed in collapsible bag have impermeabilty for vapour and liquid. The system is identical as osmotic drug delivery system. One orifice is present at the end of this formulation that helps to release the drug from compartment. The semi-permeable layer present in other compartment that used to clench osmotically active compartment containing an osmotically active salt. Absorption of water occur constantly through semi-permeable membrane to the osmotically active compartment and dissolving the osmotically component when formulation comes in contact with gastric fluid[50].

(ll). Inflatable gastrointestinal delivery system: Inflatable chamber containing liquid ether which gasifies at body temperature for inflating the chamber in stomach is incorporated. Inflatable chamber filled with a drug reservoir used for fabricating these systems. For releasing of drug reservoir with inflatable chamber the capsule dissolve after oral administration[51,52].

MECHANISM OF FLOATING SYSTEM

Because of bulk density less than gastric fluid in floating drug delivery system the drug endure buoyant in stomach with affecting gastric emptying rare for a prolonged period of time[53]. The drug is released gradually afterward the floating of

dosage form with desired rate from the system. After the release of drug the residual system is emptied from stomach[54]. The results i.e increased GRT and have a better control of fluctuation in plasma drug concentration. Apart from a minimal gastric content require for allowing the proper achievement of buoyancy retention principle , a minimal level of floating force (F) is also required for keeping the dosage form reliable buoyant on the surface of meal. If F is in positive the object float better[55].

F = F buoyancy –F gravity = (Df-Ds)gv

Where,

F= total vertical force

Df= fluid density

Ds= object density

v= volume

g= acceleration due to gravity

ADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM

Floating dosage form have various advantages:

(1). Enhancing the bioavilability and therapeutic efficacy of drugs and dose reduction e.g. Furosemide[56].

(2). The idea of FDDS are useful for development of many anti-reflux formulation[57,58].

(3). The drugs which cause mucosal irritation is reduced through slow slow release of drug at controlled rate[59].

(4). By retaining drug in GRDF at stomach preventing the degradation of drug by reducing the amount of drug reaches in colon.

(5). Floating dosage form broadly accepted for drugs having limited absorption sites in upper small intestine[60,61].

DISADVANTAGES OF FLOATING DRUG DELIVERY SYSTEM

(1). Drugs like aspirin and non-steroidal anti-inflammatory drugs cause gastric lesions , and such drugs with slow release is undesirable.

(2). Such drugs are not stable in acidic medium and irritating the stomach lining, not formulated by gastro retentive system[62].

(3). Existence of food is essential in this system for prolong their gastric emptying[63].

(4). Drugs which are fully absorb throughout the whole GI tract like Nifedipine which undergoing first pass metabolism are not good for floating drug delivery system, therefore slow gastric emptying cause decrease bioavilability.

(5). The floating system need adequately a high level of fluids in stomach for floating of drug dosage form, so that they work effectively[64].

CONCLUSION

Floating drug delivery system are applicable for drugs which have poor stability in intestinal fluid. It is useful for drugs which are degraded in intestine pH, so that drug retain in stomach for prolong period by buoyancy mechanism and give better bioavilability . Numbers of drugs which are needed to retain in stomach for their action like drugs for peptic ulcers.

REFERENCES

1. Bardronnet P, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: overview and special case of Helicobacter pylori. J Contr Rel, 2006; 111: 1-18.

2. Baviskar DT, Jain DK. Textbook of Novel Drug Delivery System. Nirali Prakashan , India: 2014; 11.1-11.13.

3. Sato Y, Kawashima Y, Takeuchi H, Yamamoto H. In- vitro and in- vivo Evaluation of riboflavin containing microballons for a Floating controlled drug delivery system in healthy human. Int. J. Pharm 2004; 275: 97-107.

4. A Badoni, A.Ojha, G.Gnanrajan, P .Kothiyal. Review on gastro retentive drug delivery system. The pharma innovation, 2012; 1(8): 32-39.

5. Rabia M., Asif M, Sana I and Umber A. Floating Drug Delivery System. International Journal of Pharmacy and Integrated Life Sciences. 2013; 1(8): 1-7.

6. Goyal T . Floating Drug Delivery Systeme. J of Curr Pharma Res, 2011 ; 5(1):7-18.

7. Hirtz J. The git absorption of drugs in man: a review of current concepts and methods of investigation. Br J Clin Pharmacol, 1985; 19:775-835.

8. Arora S, Ahuja A. Floating drug delivery system: a review. J AAPS PharmSciTech 2005;6:372-90.

9. Chien Y, Novel Drug Delivery systems., 2nd edition, Marcel Dekker, New York.(1992)

10. Bansal A, Chawla G, Gupta P & Koradia V, `Gastroretentive a means to address regional variability in intestinal drug absorption',Pharmaceutical technology,2003,pp.50-68.

11. Ponchel G, Irache JM. Specific and non-specific bioadhesive particulate system for oral delivery to the gastrointestinal tract. Adv Drug Del Rev. 1998;34:191-219.

12. Lenaerts VM, Gurny R. Gastrointestinal Tract- Physiological variables affecting the performance of oral sustained release dosage forms. In: Lenaerts V, Gurny R, eds. Bioadhesive Drug Delivery System. Boca Raton, FL: CRC Press; 1990.

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

14. C. Deepa latha, G. Vijaya lakshmi. A Review on Floating Drug delivery systems, International Journal of current Pharmaceutical Research ,2011,3(4),421-428

15. Rocca D. J.G,Omidian H, Shah K. Progresses in gastroretentive drug delivery systems, Business Briefing. Pharmatech 2003;pp 152-6.

16. Azhar Danish Khan, Meenakshi Bajpai. Floating Drug Delivery System: An overview. International Journal of pharm Tech Research, 2010;2(4):2497-2505.

17. Mayavanshi AV, Gajar SS. Floating drug delivery system to increase gastric retention of drug: A Review. J. Pharm. Res., Oct-dec. 2008: 1940:345-348.

18. Vachhani savan R, Patel Dipen, Prajapati ST, Patel CN.; J Chem.Pharma Res., 2010; 2(2):57-64.

19. Rouge N, Buri P, and Doelkar E, Drug absorption sites in the gastrointestinal tract and dosage forms for site specific delivery. Int J Pharm 1996;136:117-139.

20. Singh BN and Kim KH. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Control Release 2000; 63: 235-239.

21. Ali J, Arora S, Khar RK. Floating drug delivery system: A Review. AAPS Pharm Sci Tech 2005; 6(3): E372-E390.

22. Nagaraju K, Sushma J. A Review on floating drug delivery system. World J. Pharm. Res., 2017;6(5);553-568.

23. Dixit N. Floating Drug Delivery System. J Curr Pharm Res.2011;7(1):6-20.

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

25. Khosala R, Feely LC, Davis SS, Gastrointestinal Transit of Transit of Non Disintegrating Tablets in Fed Subject, Int J pharm, 1989;53(1):107-117.

26. Singh B, Ahuja N. Response surface optimization of drug delivery system. In Jain NK, editor. Progress in Controlled and Novel Drug Delivery System. New Delhi, India: CBS Publishers and Distributors.76-97,470-509(2004).

27. Garg S, Sharma S. Gastroretentive drug delivery system. Business Brief Pharmatech, 2003;5:36.

28. Sangekar S. Evaluation of effect of food and specific gravity of the tablets on gastric juice. Int J Pharm, 1985;35:34-53.

29. R Garg, GD Gupta, Progress in Controlled Gastro retentive Delivery Systems, Tropical Journal of Pharmaceutical Research, September, 2008; 7(3): 313-339.

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

31. Bhalla N., Goswami M. 2012. Floating Drug Delivery System. International Journal of Pharmaceutical Research and Allied Science.4,20-28.

32. Seth PR, Tossounian J. The hydrodynamically balanced system, a novel drug delivery system for oral use.Drug Dev. Ind Pharm, 1984;10:313-339.

33. Narang. N. An Updated Review On: Floating Drug Delivery System, IJAP, Vol 3, Issue 1, 2011,

34. Fix JA, Cargil R, Engle K. Gastric residence time of a non-disintegrating geometric shape in human volunteers. Pharm Res, 1995;12(3): 397-405.

35. Franz MR, Oth MP. Sustained release bilayer buoyant dosage from. United States Patent, USS5232704, 1993.

36. International Journal Of Pharmaceutical Science & Research, Bi-Layer Tablets- An Emerging Trend: A Review by Rohan D. Deshpande, et al., IJPSR, 2011;Vol. 2(10):2534-2544.

37. Streubel A, Siepmann J, Bodmeier R. Floating microparticles based on low density foam powder. Int J Pharm., 2002, 241:279-292.

38. Whitehead, L., J. Fell, and J. Collett, Development of gastroretentive dosage form. European Journal of Pharmaceutical Sciences, 1996(4): p. 74-79.

39. Jain NK. Progress in Controlled and Novel Drug Delivery Systems. First Ed. CBSS. Gopalakrishnan et al. Journal of Pharmaceutical Science and Technology. Publishers and Distributors, New Delhi Banglore 2004;3(2):84-85.

40. Goyal M, Prajapati R, Purohit KK, Mehta SC. Floating drug delivery system. Journal of current pharmaceutical research 2011; 5(1):7-18.

41. Hardenia SS, Jain A, Patel R and Kaushal A: Floating Drug Delivery Systems: A Review. Asian Journal of Pharmacy and Life Science 2011;1(3): 284-93.

42. Gupta P, Virmani K, Garg S. Hydrogels: From controlled release to pH responsive drug delivery. Drug Discovery Today 2002;7(10):569-579.

43. Roy H. M; 1976, “Drug Delivery device for preventing contact of undissolved drug with stomach lining’’, U.S. Patent.

44. Fassihi R, Yang L. Controlled release drug delivery systems. US patent 5783212. July 21, 1998.

45. Ichikawa M, Watanabe S, Miyake Y. A new multiple unit oral floating dosage system. I: Preperation and in vitro evaluation of floating and sustained release kinetics. J Pharm Sci. 1991;80:1062-1066.

46.Smart JD. The basics and underlying mechanism of mucoadhesion. Adv Drug Deliv Rev 2005;57:1556-68.

47. Desai S,``A novel floating controlled release drug delivery systems based on a dried gel matrix’’, M.S. thesis, St. John’s University, Jamaica, NY, 1984.

48. Bodmier, R. tableting of coated pellets,Eur.J.pharm biopharm, 1999, 43(1)

49. Kawashima Y, Nima T, Takeuchi H, Hino T, Itoh Y. Hollow microspheres for use as a floating controlled drug delivery system in the stomach. J Pharm Sci (USA).1998;81:135-140.

50. Michaels AS, Bashwa JD, Zaffaroni A. Integrated device for administering beneficial drug at programmed rate. United States Patent,USS3901232, 1975.

51. Jain NK. Progress in Controlled and Novel Drug Delivery Systems. 1st edition., New Delhi, India, CBS publishers and Distributors Pvt.Ltd., 2010; 76-95.

52. Bharmankar D.M.,``Biopharmaceutics and pharmacokinetics'', Vallabh prakashan, New Delhi, 335-370.

53. Makwana A, Sameja K, Parekh H, Pandya Y. Advancements in controlled release gastroretentive drug delivery system: A review. Journal of Drug Delivery & Therapeutics 2012; 2(3):12-21.

54. Sing S, Joshi V, Barpete PK. Gastroretentive drug delivery systems: Current approaches. J Pharm Res, 2009; 2(5): 881-886.

55. Moya Nakagawa, Shin-Ichikonda, YashuoiSasai,HasayukiKuzuya, Preperation of floating drug delivery system byplasma technique, Chemical and Pharmaceuticals bulletin (ThePharmaceutical society of Japan), 2006; 54(4514): 514-518.

56. Dave BS, Amin AF, Patel MM. Gastroretentive drug delivery system of ranitidine hydrochloride formulation and in vitro evaluation. AAPS Pharm. Science Technology 2004;5(2):1-6.

57. Hejazi R.,Amiji M. Chitosan-based gastrointestinal delivery systems. J Cont Rel. 2003;89, 151-165.

58. Wu W, Zhou Q, Zhang HB, Ma GD, Fu CD. Studies on nimodipine sustained release tablet capable of floating on gastric fluids with prolonged gastric resident time. Yao Xue Xue Bao. 1997;32:786-790.

59. Grabowski SR. Principles of Anatomy and Physiology. New York: JohnWilley and Sons;10;2002.

60. Chandel A, Chauhan K, Parashar B, Kumar H and Arora S: Floating drug delivery systems: A better approach. International Current Pharmaceutical Journal 2012; 1(5): 110-18.

61. Shah SH, Patel JK, Patel NV: Stomach specific floating drug delivery system: A review. International Journal of Pharmaceutical Technology and Research 2009; 1(3): 623-33.

62. Talukder R and Fissihi R. Gastroretentive Delivery Systems: A Mini review. Drug Dev and Ind Pharm 2004 ;30: 1019-1028.

63. Bharkatiya M, Kitawat S and Ojha A. Floating drug delivery system: A review. J Drug Deliv Ther. 2014; 4(2): 130-134.

64. Shweta Arora, Floating Drug Delivery Systems: A Re-view, AAPS PharmSciTech 2005; 6(3) Article 47, E.372-390.